MDLOUT , STAYED

U.S. District Court
Middle District of Florida (Tampa)
CIVIL DOCKET FOR CASE #: 8:08-cv-00213-JSM-TGW
Internal Use Only

Apotex Inc. v. Astrazeneca Pharmaceuticals LP et al
Assigned to: Judge James S. Moody, Jr
Referred to: Magistrate Judge Thomas G. Wilson
Cause: 28:2201 Declaratory Judgment

Date Filed: 01/31/2008
Date Terminated: 06/20/2008
Jury Demand: Plaintiff
Nature of Suit: 830 Patent
Jurisdiction: Federal Question

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V.

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Date Filed	#	Docket Text
01/31/2008	1	COMPLAINT against all defendants ; Jury Demand (Filing fee $ 350 receipt number T044759) filed by Apotex Inc. (Attachments: # 1 Exhibit A)(CDA) (Entered: 01/31/2008)
01/31/2008	2	Patent Report sent to Washington. (Attachments: # 1 Complaint, # 2 Exhibit A) (CDA) (Entered: 01/31/2008)
02/01/2008	3	NOTICE of designation under Local Rule 3.05 - track 2 issued by Deputy Clerk on 2/1/2008. (SMB) (Entered: 02/01/2008)
02/01/2008		(Court only) ***COPIES mailed to Counsel: Robert B. Breisblatt, J. Aron Carnahan, Laurie A. Haynie; re 3 Related case order and notice of designation of track 2 (CDA) (Entered: 02/01/2008)
02/06/2008	4	Summons issued as to Astrazeneca Pharmaceuticals LP. (CDA) (Entered: 02/06/2008)
02/08/2008	5	Unopposed MOTION for extension of time to file answer or otherwise plead re 1 Complaint by Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc.. (Guerrant, William) (Entered: 02/08/2008)

02/08/2008	6	Summons issued as to Astrazeneca UK Limited, IPR Pharmaceuticals, Inc. (CDA) (Entered: 02/11/2008)
02/13/2008	7	ENDORSED ORDER granting 5 Defendants' Motion for extension of time to answer or respond. Answers due 3/26/2008. Signed by Judge James S. Moody, Jr on 2/13/2008. (LN) (Entered: 02/13/2008)
02/13/2008		(Court only) ***COPIES mailed to Counsel: Robert B. Breisblatt, J. Aron Carnahan, Laurie A. Haynie; re 7 Order on motion for extension of time to answer (CDA) (Entered: 02/13/2008)
02/21/2008	8	*DOCUMENT TERMINATED* NOTICE by Apotex Inc. *of Filing Verified Return of Service on Defendant, Astrazeneca Pharmaceuticals* (Attachments: # 1 Exhibit A)(Fugate, Lee) COUNSEL NOTIFIED TO RE-FILE USING PROPER EVENT CODE. Modified on 2/22/2008 (CDA). (Entered: 02/21/2008)
02/22/2008	9	RETURN of service executed on 02/13/08 by Apotex Inc. as to Astrazeneca Pharmaceuticals LP. (Fugate, Lee) (Entered: 02/22/2008)
03/26/2008	10	Unopposed MOTION for Extension of Time to File Response/Reply as to 1 Complaint by Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc.. (Guerrant, William) Motions referred to Magistrate Judge Thomas G. Wilson. (Entered: 03/26/2008)
03/27/2008		(Court only) ***Motions no longer referred: 10 Unopposed MOTION for Extension of Time to File Response/Reply as to 1 Complaint (CDA) (Entered: 03/27/2008)
03/27/2008	11	ENDORSED ORDER granting 10 Defendants' Motion for Extension of Time to File Response/Reply to Plaintiff's Complaint. Responses due by 4/9/2008. Signed by Judge James S. Moody, Jr on 3/27/2008.(LAA) (Entered: 03/27/2008)
03/28/2008		(Court only) ***COPIES mailed to Counsel: Robert B. Breisblatt, J. Aron Carnahan, Laurie A. Haynie; re 11 Order on Motion for Extension of Time to File Response/Reply. (CDA) (Entered: 03/28/2008)
04/01/2008	12	NOTICE of change of address by Robert B. Breisblatt (Fugate, Lee) (Entered: 04/01/2008)
04/01/2008	13	MOTION for leave to file under seal *and Memorandum of Law in Support Thereof* by Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc.. (Tibbals, Lara) (Entered: 04/01/2008)
04/09/2008	14	NOTICE of withdrawal of motion by Astrazeneca Pharmaceuticals

		LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc. re 13 MOTION for leave to file under seal *and Memorandum of Law in Support Thereof* filed by IPR Pharmaceuticals, Inc., Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited (Tibbals, Lara) (Entered: 04/09/2008)
04/09/2008		(Court only) ***Motions terminated: 13 MOTION for leave to file under seal *and Memorandum of Law in Support Thereof* filed by IPR Pharmaceuticals, Inc., Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited. Per 14 Notice of withdrawal of motion. (CDA) (Entered: 04/09/2008)
04/09/2008	15	MOTION to dismiss Complaint *with Prejudice and Supporting Memorandum of Law* by Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc.. (Attachments: # 1 Exhibit A)(Tibbals, Lara) (Entered: 04/09/2008)
04/11/2008	16	MOTION to stay *patent action* by Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc.. (Attachments: # 1 Exhibit A)(Tibbals, Lara) (Entered: 04/11/2008)
04/14/2008		(Court only) ***Deadlines terminated. Response Deadline set for 04/09/2008 cancelled. (CDA) (Entered: 04/14/2008)
04/18/2008	17	Unopposed MOTION for Extension of Time to File Response/Reply by Apotex Inc.. (Fugate, Lee) Motions referred to Magistrate Judge Thomas G. Wilson. (Entered: 04/18/2008)
04/18/2008		(Court only) ***Motions no longer referred: 17 Unopposed MOTION for Extension of Time to File Response/Reply (CDA) (Entered: 04/18/2008)
04/21/2008	18	NOTICE by Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc. re 16 MOTION to stay *patent action* (Guerrant, William) (Entered: 04/21/2008)
04/22/2008	19	ENDORSED ORDER granting 16 Defendants' Motion for a Temporary Stay. This case shall be STAYED pending a decision by the Judicial Panel on Multidistrict Litigation on AstraZeneca's motion to transfer this case to Delaware for coordinated pretrial proceedings. The parties are directed to file a notice with this Court when a decision is reached by the JPMDL. Signed by Judge James S. Moody, Jr on 4/22/2008.(LAA) (Entered: 04/22/2008)
04/22/2008	20	ENDORSED ORDER granting 17 Unopposed Motion for Extension of Time to File Response/Reply until thirty (30) days after the stay is lifted. Signed by Judge James S. Moody, Jr on 4/22/2008.(LAA) (Entered: 04/22/2008)
04/22/2008		(Court only) ***COPIES mailed to Counsel: Robert B. Breisblatt, J.

		Aron Carnahan, Laurie A. Haynie; re 20 Order on Motion for Extension of Time to File Response/Reply, 19 Order on motion to stay. (CDA) (Entered: 04/22/2008)
06/17/2008	21	NOTICE by Astrazeneca Pharmaceuticals LP, Astrazeneca UK Limited, IPR Pharmaceuticals, Inc. re 19 Order on motion to stay (Attachments: # 1 Exhibit A)(Tibbals, Lara) (Entered: 06/17/2008)
06/20/2008	22	MULTIDISTRICT LITIGATION panel order transferring case to: District of Delaware MDL case number: 1949 (JLH) (Entered: 06/20/2008)

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC., Plaintiff, v. ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC. Defendants.	No.:

COMPLAINT FOR DECLARATORY RELIEF

Apotex Inc., for its Complaint against AstraZeneca Pharmaceuticals, LP, AstraZeneca UK Limited, and IPR Pharmaceuticals, Inc. ("Defendants") alleges as follows:

INTRODUCTION

1. This is an action for declaratory judgment of patent non-infringement under, *inter alia*, the federal Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, and 21 U.S.C. § 355(j)(5)(C)(i), which is part of the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act ("FFDCA"), as amended by Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub.L. No. 108-173, 117 Stat. 2066 (2003) ("MMA").

2. This action arises out of, *inter alia*, Apotex Inc.'s submission of an Abbreviated New Drug Application ("ANDA") to the U.S. Food and Drug Administration ("FDA") seeking approval to market a generic version of Defendants' brand-name medication CRESTOR®, known generically as rosuvastatin calcium, and used to treat high cholesterol.

PARTIES AND JURISDICTION

3. Apotex Inc. is a Canadian corporation that manufactures and sells generic drugs, with offices at 150 Signet Drive, Toronto, Canada M9L 1T9. Apotex Inc. prepared and submitted Abbreviated New Drug Application ("ANDA") No. 79-145 to the FDA for a proposed drug product consisting of rosuvastatin calcium tablets.

4. Apotex Inc. appointed Apotex Corp., whose principal place of business is located at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326, to act as Apotex Inc.'s U.S. agent for purposes of ANDA No. 79-145, under 21 C.F.R. § 314.52(c)(7)(c).

5. Upon Information and Belief after a reasonable opportunity for further investigation or discovery, there is likely to be evidentiary support that (hereafter "Upon Information and Belief") AstraZeneca Pharmaceuticals LP ("AstraZeneca") is a Delaware corporation with offices at 3000 Bayport Drive, Suite 600, Tampa, Florida 33607. Upon Information and Belief, AstraZeneca is the owner and/or assignee of U.S. Patent No. 6,316,460 ("'460 patent"), for a pharmaceutical composition which purportedly claims the drug Crestor. A copy of the '460 patent is attached as Exhibit A.

6. Upon Information and Belief, IPR Pharmaceuticals, Inc. ("IPR") is a Puerto Rico corporation with offices at Carr 188 Lote 17, San Isidro Industrial Park, Canovanas, Puerto Rico 00729. Upon Information and Belief, IPR is an affiliate or related entity of Defendant AstraZeneca Pharmaceuticals LP, and is the holder of Approved New Drug Application ("NDA") No. 021366 for rosuvastatin calcium tablets. Upon Information and Belief, AstraZeneca is IPR's authorized agent for matters related to NDA No. 021366.

7. Upon Information and Belief, AstraZeneca UK Limited ("AstraZeneca UK") is a United Kingdom corporation with offices at 15 Stanhope Gate, London W1K 1LN, England. Upon Information and Belief, AstraZeneca is a subsidiary of AstraZeneca UK Limited.

8. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a), 2201, and 21 U.S.C. § 355(j)(5)(C)(i).

9. Upon Information and Belief, personal jurisdiction over Defendants is proper because Defendants, either directly or through an affiliated entity or agent, conduct substantial business in, and have regular and systematic contact with, this District.

10. Upon Information and Belief, Defendants, either directly or through an affiliated entity or agent, maintain a continuous and systematic contact with the State of Florida and this District by conducting substantial, regular and systematic business therein through, *inter alia*, maintaining business offices in this District and through the marketing and sale of pharmaceutical products, including Crestor—the purported commercial embodiment of the patent in suit.

11. Upon Information and Belief, the conduct of Defendants, either directly or through an affiliated entity or agent, is such that assertion of personal jurisdiction over Defendants is reasonable and fair.

12. Upon Information and Belief, Defendants, either directly or through a related entity or agent, purposely avail themselves of the privilege of doing business in the State of Florida and in this District.

13. Venue is proper in this district under 28 U.S.C. §§ 1391(c), 1391(d), 1400(b), and 21 U.S.C. § 355(j)(5)(C)(i)(II).

BACKGROUND

14. Upon Information and Belief, Defendants purport to own all substantial rights in, and purport to have the right to sue for infringement of, the '460 patent. Upon submission by Defendants, the '460 patent was listed in the FDA's compilation of approved drugs and their respective patents entitled "Approved Drugs With Therapeutic Equivalence Evaluations," commonly referred to as the "Orange Book." As a consequence of such Orange Book listing, Defendants maintain, and have affirmatively represented to the world, that the '460 patent claims the approved drug Crestor®, and that a claim for patent infringement could reasonably be asserted against any generic ANDA applicant, including Apotex Inc., attempting to market a generic rosuvastatin calcium product before the expiration of the '460 patent.

15. On Information and Belief, Defendants hold all substantial rights in the '460 patent and have the right to sue for infringement thereof.

16. Apotex Inc. has submitted an Abbreviated New Drug Application ("ANDA") to the U.S. Food and Drug Administration ("FDA") seeking approval to market a generic version of Defendants' brand name medication Crestor, known generically as rosuvastatin calcium, ANDA No. 79-145, in which Apotex Inc. seeks to market a generic rosuvastatin product before the expiration of the '460 patent.

17. In ANDA No. 79-145, as amended, Apotex Inc. has certified, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that its proposed rosuvastatin tablets will not infringe the '460 patent.

18. Apotex Inc.'s submission of the paragraph IV certifications to the '460 patent puts Apotex Inc. at considerable risk of being sued by Defendants both before and after market entry.

19. In a letter dated November 5, 2007, Apotex Inc. sent to AstraZeneca a certification under 21 U.S.C. § 355(j)(2)(B)(i) and (ii) that the FDA had received an ANDA submitted by Apotex Inc. certifying the noninfringement of the '460 patent. Over 45 days have passed, and Defendants have not sued Apotex Inc. for infringement of the '460 patent.

20. There is an actual, substantial and continuing justiciable case and controversy between Apotex Inc. and Defendants regarding the '460 patent, over which this Court can and should exercise jurisdiction and declare the rights of the parties. Apotex Inc. is entitled by law to bring and maintain this action for declaratory judgment of patent-non infringement under the Declaratory Judgment Act and the MMA where, as here, Defendants did not sue Apotex Inc. within 45 days of receipt of Apotex Inc.'s notice of paragraph IV certification to the '460 patent, and Apotex Inc. has offered Defendants an Offer of Confidential Access to Apotex Inc.'s ANDA for generic rosuvastatin calcium.

COUNT I – DECLARATORY RELIEF

21. Apotex Inc. incorporates by reference paragraphs 1-20 of this Complaint as if fully set forth herein.

22. Apotex Inc. cannot be held liable for infringement of the '460 patent because the claims of the patent are limited to a composition comprising a tribasic phosphate salt in which the cation is multivalent, and Apotex Inc.'s tablets will not comprise a tribasic phosphate salt in which the cation is multivalent or an obvious equivalent.

23. As a consequence of the foregoing, there exists a justiciable controversy as to whether the '460 patent is infringed. Apotex Inc. is entitled to a declaration that the '460 patent is not infringed.

DEMAND FOR JUDGMENT AND PRAYER FOR RELIEF

WHEREFORE, Apotex Inc. prays for judgment:

A. Finding that the '460 patent is not infringed;

B. Finding that this is an exceptional case under 35 U.S.C. § 285;

C. Awarding Apotex Inc. its costs, expenses, and reasonable attorney's fees; and

D. Awarding such other relief as the Court deems just and appropriate.

JURY DEMAND

Apotex Inc. demands a trial by jury for all issues triable by a jury.

Dated: January 31, 2008

Respectfully submitted,

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Of Counsel for Plaintiff Apotex Inc.

US006316460B1

(12) **United States Patent**
Creekmore et al.

(10) **Patent No.: US 6,316,460 B1**
(45) **Date of Patent: Nov. 13, 2001**

(54) **PHARMACEUTICAL COMPOSITIONS**

(75) Inventors: **Joseph R Creekmore; Norman A. Wiggins**, both of Wilmington, DE (US)

(73) Assignee: **Astrazeneca AB**, Sodertalje (SE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/633,064**

(22) Filed: **Aug. 4, 2000**

(30) **Foreign Application Priority Data**

Jan. 26, 2000 (GB) 0001621

(51) **Int. Cl.**[7] **A61K 31/505**; A61K 31/19
(52) **U.S. Cl.** **514/275**; 514/256; 514/557
(58) **Field of Search** 514/557, 256, 514/275

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,743,450	5/1988	Harris et al. .
5,260,440	11/1993	Hirai et al. .
5,356,896	10/1994	Kabadi et al. .
5,665,881	9/1997	Inoue et al. .
5,686,104	11/1997	Mills et al. .
6,150,410	11/2000	Engh et al. .

FOREIGN PATENT DOCUMENTS

0 336 298	3/1988	(EP) .
0 380 021	8/1990	(EP) .
0 475 482 A1	3/1992	(EP) .
0 521 471	1/1993	(EP) .
2 262 229	6/1993	(GB) .
WO 97/23200	7/1997	(WO) .
WO 99/62560	12/1999	(WO) .
WO 00/35425	6/2000	(WO) .
WO 00/42024	7/2000	(WO) .
WO 00/45817	8/2000	(WO) .
WO 00/45818	8/2000	(WO) .
WO 00/45819	8/2000	(WO) .

OTHER PUBLICATIONS

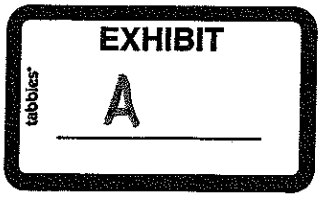
Remington's Pharmaceutical Sciences, 13th Ed., 1965, left –hand column, lines 25–27.

Primary Examiner—Zohreh Fay
Assistant Examiner—Brian-Yong Kwon
(74) *Attorney, Agent, or Firm*—Pillsbury Winthrop LLP

(57) **ABSTRACT**

The invention concerns a pharmaceutical composition comprising the HMG CoA reductase inhibitor (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, which remains stable over a prolonged period.

18 Claims, No Drawings



PHARMACEUTICAL COMPOSITIONS

CROSS-REFERENCES TO RELATED APPLICATIONS

Not Applicable

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

Not Applicable.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to pharmaceutical compositions and more particularly to a pharmaceutical composition containing (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhyhept-6-enoic acid or a pharmaceutically acceptable salt thereof (and referred to hereinafter as "the Agent"), in particular the sodium and calcium salts, and especially the calcium salt, bis[(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid] calcium salt (of the formula I hereinafter).

2. Description of the Related Art

The Agent is disclosed as an inhibitor of 3-hydroxy-3-methylglutaryl CoA reductase (HMG CoA reductase) in European Patent Application, Publication No. 0521471 and in Bioorganic and Medicinal Chemistry, (1997), 5(2), 437–444 and is useful in the treatment of hypercholesterolemia, hyperlipidproteinemia and atherosclerosis.

A problem associated with the Agent is that it undergoes degradation under certain conditions. This makes it difficult to formulate the product and provide a pharmaceutical composition with adequate storage life. The major degradation products formed are the corresponding (3R,5S) lactone (hereinafter referred to as "the lactone") and an oxidation product (hereinafter referred to as "B2") in which the hydroxy group adjacent to the carbon-carbon double bond is oxidised to a ketone functionality.

It is therefore important to find a pharmaceutical composition of the Agent which remains stable over a prolonged period. It is also preferable that such a composition has a good flow rate to assist processing into unit dosage forms for oral administration, for example into tablets, and good disintegration and dissolution characteristics when processed into tablets for oral administration, which tablets can be in different dosage strengths. It is also desirable that such tablets are of a convenient size for ease of administration.

Pharmaceutical formulations of certain 7-substituted-3,5-dihydroxy-6-heptenoic acid salts, which are HMG CoA reductase inhibitors, are disclosed in UK Patent 2262229.

These formulations require the presence of an alkaline medium (such as a carbonate or bicarbonate) capable of imparting a pH of at least 8 to an aqueous solution or dispersion of the composition.

BRIEF SUMMARY OF THE INVENTION

We have now discovered a novel pharmaceutical composition of the Agent which has advantageous properties and which solves one or more of the problems associated with formulation of the Agent.

Accordingly, a first aspect of the invention comprises a pharmaceutical composition comprising the Agent and a tribasic phosphate salt in which the cation is multivalent.

A second aspect of the invention comprises the use of a tribasic phosphate salt in which the cation is multivalent to stabilise the Agent.

DETAILED DESCRIPTION OF THE INVENTION

A tribasic phosphate salt in which the cation is multivalent includes, for example, tribasic calcium phosphate, tribasic magnesium phosphate and tribasic aluminum phosphate. Tribasic calcium phosphate is especially preferred.

The ratio of tribasic phosphate salt to Agent in the pharmaceutical composition is, for example, within the range of 1:80 to 50:1 by weight, for example 1:50 to 50:1 by weight, such as 1:10 to 10:1 by weight, and more particularly 1:5 to 10:1by weight.

Preferably the pharmaceutical composition of the invention is formulated into an oral dosage form, such as a tablet. Accordingly a further aspect of the invention comprises a pharmaceutical composition comprising the Agent, a tribasic phosphate salt in which the cation is multivalent, and one or more fillers, binders, disintegrates or lubricants. A still further aspect of the invention relates to a pharmaceutical composition for oral administration comprising the Agent, one or more fillers, one or more binders, one or more disintegrates, one or more lubricants and a tribasic phosphate salt in which the cation is multivalent.

Suitable fillers include, for example, lactose, sugar, starches, modified starches, mannitol, sorbitol, inorganic salts, cellulose derivatives (e.g. microcrystalline cellulose, cellulose), calcium sulfate, xylitol and lactitol.

Suitable binders include, for example, polyvinylpyrrolidone, lactose, starches, modified starches, sugars, gum acacia, gum tragacanth, guar gum, pectin, wax binders, microcrystalline cellulose, methylcellulose, carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, copolyvidone, gelatin and sodium alginate.

Suitable disintegrates include, for example, crosscarmellose sodium, crospovidone, polyvinylpyrrolidone, sodium starch glycollate, corn starch, microcrystalline cellulose, hydroxypropyl methylcellulose and hydroxypropyl cellulose.

Suitable lubricants include, for example, magnesium stearate, stearic acid, palmitic acid, calcium stearate, talc, carnauba wax, hydrogenated vegetable oils, mineral oil, polyethylene glycols and sodium stearyl fumarate.

Additional conventional excipients which may be added include preservatives, stabilisers, anti-oxidants, silica flow conditioners, antiadherents or glidants.

Other suitable fillers, binders, disintegrates, lubricants and additional excipients which may be used are described in *Handbook of Pharmaceutical Excipients*, 2nd Edition, American Pharmaceutical Association; *The Theory and Practice of Industrial Pharmacy*, 2nd Edition, Lachman, Leon, 1976; *Pharmaceutical Dosage Forms*: Tablets Volume 1, 2nd Edition, Lieberman, Hebert A., et al, 1989; *Modern Pharmaceutics, Banker*, Gilbert and Rhodes, Christopher T, 1979; and *Remington's Pharmaceutical Sciences*, 15th Edition, 1975.

Typically the Agent will be present in an amount within the range of 1 to 50%, and preferably from 1 to 20% (especially 2 to 15%) by weight of the composition.

Typically the tribasic phosphate salt, such as tribasic calcium phosphate, will be present in an amount within the range of 1 to 50%, for example 1 to 25%, such as 1 to 20%, and particularly 5 to 18% by weight.

Typically one or more fillers will be present in an amount 30 to 90% by weight.

Typically one or more binders will be present in an amount 2 to 90% by weight.

Typically one or more disintegrates will be present in an amount 2 to 10%, and especially 4 to 6% by weight.

It will be appreciated that a particular excipient may act as both a binder and a filler, or as a binder, a filler and a disintegrant. Typically the combined amount of filler, binder and disintegrant comprises, for example, 70 to 90% by weight of the composition.

Typically one or more lubricants will be present in an amount 0.5 to 3%, and especially 1 to 2% by weight.

Preferred compositions of the invention include, for example, those comprising the Agent, tribasic calcium phosphate and excipients selected from lactose, mannitol, microcrystalline cellulose, povidone, crospovidone, sodium starch glycollate and magnesium stearate. Preferred independent compositions of the invention include, for example, compositions comprising the Agent, tribasic calcium phosphate, microcrystalline cellulose, lactose, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate; compositions comprising the Agent, povidone, tribasic calcium phosphate, microcrystalline cellulose, mannitol, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate; compositions comprising the Agent, tribasic calcium phosphate, crospovidone, microcrystalline cellulose, lactose and magnesium stearate, and compositions comprising the Agent, povidone, tribasic calcium phosphate, microcrystalline cellulose, lactose, sodium starch glycollate, magnesium stearate and butylated hydroxytoluene. Where lactose and microcrystalline cellulose are used, these are preferably present in the ratio of about 1:1 to 3:1 by weight.

Compositions of the invention which are of particular interest include, for example, the specific embodiments set out hereinafter in the accompanying Examples.

The pharmaceutical composition of the invention may be prepared, using standard techniques and manufacturing processes generally known in the art, for example by dry blending the components. For example, the Agent, the tribasic phosphate salt (for example tribasic calcium phosphate), one or more fillers, one or more binders and one or more disintegrates, as well as other additional excipients if desired are blended together. The components of the blend prior to blending, or the blend itself, may be passed through a mesh screen, for example a 400–700 um mesh screen. A lubricant, which may also be screened, is then added to the blend and blending continued until a homogeneous mixture is obtained. The mixture is then compressed into tablets. Alternatively, a wet granulation technique can be employed. For example, the Agent, the tribasic phosphate salt, one or more fillers, one or more binders and a portion of a disintegrant, as well as other additional excipients if desired, are blended together, for example by using a granulator, and the powder blend is granulated with a small volume of purified water. The granulate is dried and passed though a mill. The remainder of the disintegrant and a lubricant are added to the milled granulation and after blending the resultant homogeneous mixture is compressed into tablets. It will be appreciated that modifications of the dry blending and wet granulation techniques, including the order of addition of the components and their screening and blending prior to compression into tablets, may be carried out according to principles well known in the art.

A tablet coating may then be applied, for example by spray-coating. With a water-based film coating formulation.

The coating may comprise, for example, lactose, hydroxypropyl methylcellulose, triacetin, titanium dioxide and ferric oxides. Coating ingredient combinations are commercially available, such as those described in the Examples hereinafter. The coating may comprise, for example, 0.5 to 10% by weight of the tablet composition, particularly 1 to 6%, and preferably 2 to 3%. Coatings containing ferric oxides are especially preferred as they reduce the rate of formation of photodegradation products of the Agent.

A further aspect of the present invention comprises a method of preparing a stabilised pharmaceutical composition which comprises admixing the Agent with a tribasic phosphate salt in which the cation is multivalent. A further aspect of the present invention comprises a method of producing a stabilised pharmaceutical composition which comprises incorporating a tribasic phosphate salt in which the cation is multivalent in a pharmaceutical composition containing the Agent.

The following pharmaceutical compositions, wherein the Agent is the calcium salt of formula I, are intended to illustrate the invention without being limitative in any way.

EXAMPLE 1

The Agent	2.50 mg
Tribasic calcium phosphate	20.0 mg
Microcrystalline cellulose	47.0 mg
Lactose monohydrate	47.0 mg
Sodium starch glycollate	3.00 mg
Butylated hydroxytoluene	0.05 mg
Magnesium stearate	1.00 mg

The Agent, microcrystalline cellulose, lactose monohydrate, sodium starch glycolate, tribasic calcium phosphate, and butylated hydroxytoluene were blended together for 10 minutes. Magnesium stearate was screened through a #40 mesh (425 um) screen and added to the blend and blending continued for a further three minutes. The resulting homogeneous mixture was compressed into tablets.

The tablets were stored at 70° C./80% relative humidity for one week. After one week there was found to be only 0.11% w/w of the oxidation product B2 formed and only 0.50% w/w of the lactone. By comparison a similar formulation in which 20.0 mg of tribasic calcium phosphate was replaced by 20.0 mg of dibasic calcium phosphate, 0.23% w/w of B2 was formed and 15.61% w/w of the lactone.

EXAMPLE 2

The Agent	2.50 mg
Povidone	2.50 mg
Tribasic calcium phosphate	20.0 mg
Microcrystalline cellulose	47.0 mg
Mannitol	47.0 mg
Sodium starch glycollate	3.00 mg
Butylated hydroxytoluene	0.05 mg
Magnesium stearate	1.00 mg

The Agent, povidone, mannitol, microcrystalline cellulose, butylated hydroxytoluene, tribasic calcium phosphate and sodium starch glycollate (in the amounts given above) were blended for 5 to 60 minutes. Magnesium stearate was screened through a #40 mesh (425 um) screen

and added to the blend and blending continued for a further three minutes. The resulting homogeneous mixture was compressed into tablets. The compressed tablets were coated by spraying with a mixture of hydroxypropyl methylcellulose, polyethylene glycol 400, titanium dioxide and ferric oxide (sold as Spectrablend by Warner-Jenkinson) and water in a coating pan. The weight gain provided by the coating was 1 to 6% w/w, and preferably 2 to 3% w/w.

The tablets were stored at 70° C./80% relative humidity for one week. After one week here was found to be only 0.06% w/w of the oxidation product B2 formed and only 2.22% w/w of the lactone.

EXAMPLE 3

The Agent	2.60 mg
Crospovidone	3.75 mg
Tribasic calcium phosphate	5.66 mg
Microcrystalline cellulose	15.5 mg
Lactose monohydrate	46.5 mg
Magnesium stearate	0.94 mg

The Agent and crospovidone were blended together for 5 minutes and the blend then passed through a 400–700 um screen. A small portion of the microcrystalline cellulose was passed through the screen afterwards. The screened material was blended with the other ingredients, excluding the lubricant, for 10 minutes. Magnesium stearate was passed through a #40 mesh (425 um) screen and added to the blend and the mixture was blended for a further 3 minutes. The resulting homogeneous mixture was compressed into tablets. The compressed tablets were coated by spraying with a mixture of lactose monohydrate, hydroxypropyl methylcellulose, triacetin and ferric oxide (sold as Opadry II by Colorcon) and water in a coating pan. The weight gain provided by the coating 1 to 6% w/w, and preferably 2 to 3% w/w.

The tablets were stored at 70° C./80% relative humidity for one week. After this time only 0.19% w/w of the oxidation product B2 had formed and only 2.71% w/w of the lactone.

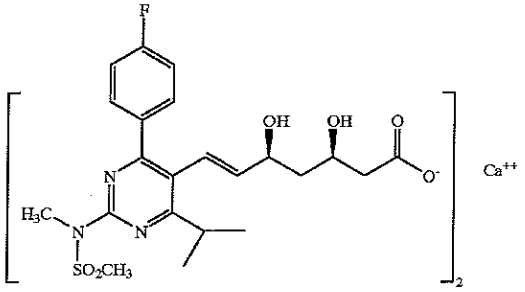
EXAMPLE 4

The Agent	2.50 mg
Povidone	2.50 mg
Tribasic calcium phosphate	20.0 mg
Microcrystalline cellulose	34.5 mg
Lactose monohydrate	34.0 mg
Sodium starch glycollate	6.00 mg
Magnesium stearate	1.00 mg
Butylated hydroxytoluene	0.05 mg

A portion of the tribasic calcium phosphate and butylated hydroxytoluene were blended for 30 seconds in a bag. The Agent, povidone, remainder of the tribasic calcium phosphate, microcrystalline cellulose, lactose monohydrate, tribasic calcium phophate/butylated hydroxytoluene mixture and a portion of the sodium starch glycolate were blended in a granulator for 30 seconds. The powder blend was granulated with purified water for 1 minute at the addition rate of 70 mg/tablet/minute. The granulation is dried in a fluidized bed drier at 50° C. until the loss on drying is less than 2% w/w. The dried granulation is passed through a mill (e.g. Comil). The milled granulation and the remainder of the sodium starch glycolate was blended for approximately 5 minutes. Magnesium stearate was screened through a #40 mesh (425 um) screen and added to the blend and blending continued for a further three minutes. The resulting homogeneous mixture was compressed into tablets.

The tablets were stored at 70° C./80% relative humidity for one week. After this time only 0.23% w/w of the oxidation product B2 had formed and only 0.28% w/w of the lactone. by comparison a similar formulation in which 20.0 mg of tribasic calcium phosphate was replaced by 20.0 mg of dibasic calcium phosphate, 0.19% w/w of B2 was formed and 28.15% w/w of the lactone.

Formula 1



What we claim is:

1. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient and a tribasic phosphate salt in which the cation is multivalent.

2. The pharmaceutical composition as claimed in claim 1 wherein the tribasic phosphate salt in which the cation is multivalent is selected from the group consisting of tribasic calcium phosphate, tribasic magnesium phosphate and tribasic aluminum phosphate.

3. The pharmaceutical composition as claimed in claim 1 or 2 wherein the tribasic phosphate salt in which the cation is multivalent is tribasic calcium phosphate.

4. The pharmaceutical composition as claimed in claim 1 or 2 wherein the ratio of the tribasic phosphate salt to the active ingredient is in the range of 1:80 to 50:1 by weight.

5. The pharmaceutical composition as claimed in claim 1 or 2 additionally comprising one or more fillers, binders, disintegrates or lubricants.

6. A pharmaceutical composition for oral administration comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, one or more fillers, one or more binders, one or more disintegrants, one or more lubricants and a tribasic phosphate salt in which the cation is multivalent.

7. The pharmaceutical composition as claimed in claim 6 wherein the active ingredient is present in an amount 1 to 80% by weight of the composition.

8. The pharmaceutical composition as claimed in claim 6 or 7 wherein the tribasic phosphate salt is present in an amount 1 to 50% by weight of the composition.

9. The pharmaceutical composition as claimed in claim 6 or 7 wherein the filler is present in an amount 30 to 90% by weight of the composition.

10. The pharmaceutical composition as claimed in claim 6 or 7 wherein the binder is present in an amount 2 to 90% by weight of the composition.

11. The pharmaceutical composition as claimed in claim 6 or 7 wherein the disintegrant is present in an amount 2 to 10% by weight of the composition.

12. The pharmaceutical composition as claimed in claim 6 or 7 wherein the lubricant is present in an amount 0.5 to 3% by weight.

13. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, microcrystalline cellulose, lactose, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate.

14. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, microcrystalline cellulose, mannitol, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate.

15. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, crospovidone, microcrystalline cellulose, lactose and magnesium stearate.

16. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, povidone, microcrystalline cellulose, lactose, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate.

17. The pharmaceutical composition as claimed in claim 1, 2, 6, 13, 14, 15 or 16 wherein the active ingredient is the calcium salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5- dihydroxyhept-6-enoic acid.

18. A method of producing a stabilised pharmaceutical composition, said method comprising the step of incorporating a tribasic phosphate salt in which the cation is multivalent in a pharmaceutical composition containing the compound (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl (methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof.

* * * * *

AO 120 (Rev. 3/04)

TO:		
	Mail Stop 8 **Director of the U.S. Patent and Trademark Office** **P.O. Box 1450** **Alexandria, VA 22313-1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court Middle District of Florida, Tampa on the following X Patents or ☐ Trademarks:

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
8:08-cv-213-T-30TGW	1/31/2008	Middle District of Florida - Tampa Division

PLAINTIFF	DEFENDANT
Apotex Inc.	Astrazeneca Pharmaceuticals LP; Astrazeneca UK Limited; and IPR Pharmaceuticals, Inc.

	PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1	See attached complaint		
2			
3			
4			
5			

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
2		
3		
4		
5		

In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
Sheryl L. Loesch	s/ Carrie Davis Ayers	1/31/2008

Copy 1—Upon initiation of action, mail this copy to Director Copy 3—Upon termination of action, mail this copy to Director
Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy

US006316460B1

(12) **United States Patent**
Creekmore et al.

(10) **Patent No.: US 6,316,460 B1**
(45) **Date of Patent: Nov. 13, 2001**

(54) **PHARMACEUTICAL COMPOSITIONS**

(75) Inventors: **Joseph R Creekmore; Norman A. Wiggins**, both of Wilmington, DE (US)

(73) Assignee: **Astrazeneca AB**, Sodertalje (SE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/633,064**

(22) Filed: **Aug. 4, 2000**

(30) **Foreign Application Priority Data**

Jan. 26, 2000 (GB) 0001621

(51) **Int. Cl.**[7] **A61K 31/505**; A61K 31/19
(52) **U.S. Cl.** **514/275**; 514/256; 514/557
(58) **Field of Search** 514/557, 256, 514/275

(56) **References Cited**

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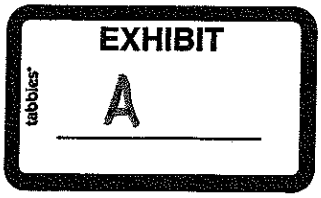
Primary Examiner—Zohreh Fay
Assistant Examiner—Brian-Yong Kwon
(74) *Attorney, Agent, or Firm*—Pillsbury Winthrop LLP

(57) **ABSTRACT**

The invention concerns a pharmaceutical composition comprising the HMG CoA reductase inhibitor (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, which remains stable over a prolonged period.

18 Claims, No Drawings



PHARMACEUTICAL COMPOSITIONS

CROSS-REFERENCES TO RELATED APPLICATIONS

Not Applicable

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

Not Applicable.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to pharmaceutical compositions and more particularly to a pharmaceutical composition containing (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhyhept-6-enoic acid or a pharmaceutically acceptable salt thereof (and referred to hereinafter as "the Agent"), in particular the sodium and calcium salts, and especially the calcium salt, bis[(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid] calcium salt (of the formula I hereinafter).

2. Description of the Related Art

The Agent is disclosed as an inhibitor of 3-hydroxy-3-methylglutaryl CoA reductase (HMG CoA reductase) in European Patent Application, Publication No. 0521471 and in Bioorganic and Medicinal Chemistry, (1997), 5(2), 437–444 and is useful in the treatment of hypercholesterolemia, hyperlipidproteinemia and atherosclerosis.

A problem associated with the Agent is that it undergoes degradation under certain conditions. This makes it difficult to formulate the product and provide a pharmaceutical composition with adequate storage life. The major degradation products formed are the corresponding (3R,5S) lactone (hereinafter referred to as "the lactone") and an oxidation product (hereinafter referred to as "B2") in which the hydroxy group adjacent to the carbon-carbon double bond is oxidised to a ketone functionality.

It is therefore important to find a pharmaceutical composition of the Agent which remains stable over a prolonged period. It is also preferable that such a composition has a good flow rate to assist processing into unit dosage forms for oral administration, for example into tablets, and good disintegration and dissolution characteristics when processed into tablets for oral administration, which tablets can be in different dosage strengths. It is also desirable that such tablets are of a convenient size for ease of administration.

Pharmaceutical formulations of certain 7-substituted-3,5-dihydroxy-6-heptenoic acid salts, which are HMG CoA reductase inhibitors, are disclosed in UK Patent 2262229.

These formulations require the presence of an alkaline medium (such as a carbonate or bicarbonate) capable of imparting a pH of at least 8 to an aqueous solution or dispersion of the composition.

BRIEF SUMMARY OF THE INVENTION

We have now discovered a novel pharmaceutical composition of the Agent which has advantageous properties and which solves one or more of the problems associated with formulation of the Agent.

Accordingly, a first aspect of the invention comprises a pharmaceutical composition comprising the Agent and a tribasic phosphate salt in which the cation is multivalent.

A second aspect of the invention comprises the use of a tribasic phosphate salt in which the cation is multivalent to stabilise the Agent.

DETAILED DESCRIPTION OF THE INVENTION

A tribasic phosphate salt in which the cation is multivalent includes, for example, tribasic calcium phosphate, tribasic magnesium phosphate and tribasic aluminum phosphate. Tribasic calcium phosphate is especially preferred.

The ratio of tribasic phosphate salt to Agent in the pharmaceutical composition is, for example, within the range of 1:80 to 50:1 by weight, for example 1:50 to 50:1 by weight, such as 1:10 to 10:1 by weight, and more particularly 1:5 to 10:1by weight.

Preferably the pharmaceutical composition of the invention is formulated into an oral dosage form, such as a tablet. Accordingly a further aspect of the invention comprises a pharmaceutical composition comprising the Agent, a tribasic phosphate salt in which the cation is multivalent, and one or more fillers, binders, disintegrates or lubricants. A still further aspect of the invention relates to a pharmaceutical composition for oral administration comprising the Agent, one or more fillers, one or more binders, one or more disintegrates, one or more lubricants and a tribasic phosphate salt in which the cation is multivalent.

Suitable fillers include, for example, lactose, sugar, starches, modified starches, mannitol, sorbitol, inorganic salts, cellulose derivatives (e.g. microcrystalline cellulose, cellulose), calcium sulfate, xylitol and lactitol.

Suitable binders include, for example, polyvinylpyrrolidone, lactose, starches, modified starches, sugars, gum acacia, gum tragacanth, guar gum, pectin, wax binders, microcrystalline cellulose, methylcellulose, carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, copolyvidone, gelatin and sodium alginate.

Suitable disintegrates include, for example, crosscarmellose sodium, crospovidone, polyvinylpyrrolidone, sodium starch glycollate, corn starch, microcrystalline cellulose, hydroxypropyl methylcellulose and hydroxypropyl cellulose.

Suitable lubricants include, for example, magnesium stearate, stearic acid, palmitic acid, calcium stearate, talc, carnauba wax, hydrogenated vegetable oils, mineral oil, polyethylene glycols and sodium stearyl fumarate.

Additional conventional excipients which may be added include preservatives, stabilisers, anti-oxidants, silica flow conditioners, antiadherents or glidants.

Other suitable fillers, binders, disintegrates, lubricants and additional excipients which may be used are described in *Handbook of Pharmaceutical Excipients*, 2nd Edition, American Pharmaceutical Association; *The Theory and Practice of Industrial Pharmacy*, 2nd Edition, Lachman, Leon, 1976; *Pharmaceutical Dosage Forms*: Tablets Volume 1, 2nd Edition, Lieberman, Hebert A., et al, 1989; *Modern Pharmaceutics, Banker*, Gilbert and Rhodes, Christopher T, 1979; and *Remington's Pharmaceutical Sciences*, 15th Edition, 1975.

Typically the Agent will be present in an amount within the range of 1 to 50%, and preferably from 1 to 20% (especially 2 to 15%) by weight of the composition.

Typically the tribasic phosphate salt, such as tribasic calcium phosphate, will be present in an amount within the range of 1 to 50%, for example 1 to 25%, such as 1 to 20%, and particularly 5 to 18% by weight.

Typically one or more fillers will be present in an amount 30 to 90% by weight.

Typically one or more binders will be present in an amount 2 to 90% by weight.

Typically one or more disintegrates will be present in an amount 2 to 10%, and especially 4 to 6% by weight.

It will be appreciated that a particular excipient may act as both a binder and a filler, or as a binder, a filler and a disintegrant. Typically the combined amount of filler, binder and disintegrant comprises, for example, 70 to 90% by weight of the composition.

Typically one or more lubricants will be present in an amount 0.5 to 3%, and especially 1 to 2% by weight.

Preferred compositions of the invention include, for example, those comprising the Agent, tribasic calcium phosphate and excipients selected from lactose, mannitol, microcrystalline cellulose, povidone, crospovidone, sodium starch glycollate and magnesium stearate. Preferred independent compositions of the invention include, for example, compositions comprising the Agent, tribasic calcium phosphate, microcrystalline cellulose, lactose, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate; compositions comprising the Agent, povidone, tribasic calcium phosphate, microcrystalline cellulose, mannitol, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate; compositions comprising the Agent, tribasic calcium phosphate, crospovidone, microcrystalline cellulose, lactose and magnesium stearate, and compositions comprising the Agent, povidone, tribasic calcium phosphate, microcrystalline cellulose, lactose, sodium starch glycollate, magnesium stearate and butylated hydroxytoluene. Where lactose and microcrystalline cellulose are used, these are preferably present in the ratio of about 1:1 to 3:1 by weight.

Compositions of the invention which are of particular interest include, for example, the specific embodiments set out hereinafter in the accompanying Examples.

The pharmaceutical composition of the invention may be prepared, using standard techniques and manufacturing processes generally known in the art, for example by dry blending the components. For example, the Agent, the tribasic phosphate salt (for example tribasic calcium phosphate), one or more fillers, one or more binders and one or more disintegrates, as well as other additional excipients if desired are blended together. The components of the blend prior to blending, or the blend itself, may be passed through a mesh screen, for example a 400–700 um mesh screen. A lubricant, which may also be screened, is then added to the blend and blending continued until a homogeneous mixture is obtained. The mixture is then compressed into tablets. Alternatively, a wet granulation technique can be employed. For example, the Agent, the tribasic phosphate salt, one or more fillers, one or more binders and a portion of a disintegrant, as well as other additional excipients if desired, are blended together, for example by using a granulator, and the powder blend is granulated with a small volume of purified water. The granulate is dried and passed though a mill. The remainder of the disintegrant and a lubricant are added to the milled granulation and after blending the resultant homogeneous mixture is compressed into tablets. It will be appreciated that modifications of the dry blending and wet granulation techniques, including the order of addition of the components and their screening and blending prior to compression into tablets, may be carried out according to principles well known in the art.

A tablet coating may then be applied, for example by spray-coating. With a water-based film coating formulation.

The coating may comprise, for example, lactose, hydroxypropyl methylcellulose, triacetin, titanium dioxide and ferric oxides. Coating ingredient combinations are commercially available, such as those described in the Examples hereinafter. The coating may comprise, for example, 0.5 to 10% by weight of the tablet composition, particularly 1 to 6%, and preferably 2 to 3%. Coatings containing ferric oxides are especially preferred as they reduce the rate of formation of photodegradation products of the Agent.

A further aspect of the present invention comprises a method of preparing a stabilised pharmaceutical composition which comprises admixing the Agent with a tribasic phosphate salt in which the cation is multivalent. A further aspect of the present invention comprises a method of producing a stabilised pharmaceutical composition which comprises incorporating a tribasic phosphate salt in which the cation is multivalent in a pharmaceutical composition containing the Agent.

The following pharmaceutical compositions, wherein the Agent is the calcium salt of formula I, are intended to illustrate the invention without being limitative in any way.

EXAMPLE 1

The Agent	2.50 mg
Tribasic calcium phosphate	20.0 mg
Microcrystalline cellulose	47.0 mg
Lactose monohydrate	47.0 mg
Sodium starch glycollate	3.00 mg
Butylated hydroxytoluene	0.05 mg
Magnesium stearate	1.00 mg

The Agent, microcrystalline cellulose, lactose monohydrate, sodium starch glycolate, tribasic calcium phosphate, and butylated hydroxytoluene were blended together for 10 minutes. Magnesium stearate was screened through a #40 mesh (425 um) screen and added to the blend and blending continued for a further three minutes. The resulting homogeneous mixture was compressed into tablets.

The tablets were stored at 70° C./80% relative humidity for one week. After one week there was found to be only 0.11% w/w of the oxidation product B2 formed and only 0.50% w/w of the lactone. By comparison a similar formulation in which 20.0 mg of tribasic calcium phosphate was replaced by 20.0 mg of dibasic calcium phosphate, 0.23% w/w of B2 was formed and 15.61% w/w of the lactone.

EXAMPLE 2

The Agent	2.50 mg
Povidone	2.50 mg
Tribasic calcium phosphate	20.0 mg
Microcrystalline cellulose	47.0 mg
Mannitol	47.0 mg
Sodium starch glycollate	3.00 mg
Butylated hydroxytoluene	0.05 mg
Magnesium stearate	1.00 mg

The Agent, povidone, mannitol, microcrystalline cellulose, butylated hydroxytoluene, tribasic calcium phosphate and sodium starch glycollate (in the amounts given above) were blended for 5 to 60 minutes. Magnesium stearate was screened through a #40 mesh (425 um) screen

and added to the blend and blending continued for a further three minutes. The resulting homogeneous mixture was compressed into tablets. The compressed tablets were coated by spraying with a mixture of hydroxypropyl methylcellulose, polyethylene glycol 400, titanium dioxide and ferric oxide (sold as Spectrablend by Warner-Jenkinson) and water in a coating pan. The weight gain provided by the coating was 1 to 6% w/w, and preferably 2 to 3% w/w.

The tablets were stored at 70° C./80% relative humidity for one week. After one week here was found to be only 0.06% w/w of the oxidation product B2 formed and only 2.22% w/w of the lactone.

EXAMPLE 3

The Agent	2.60 mg
Crospovidone	3.75 mg
Tribasic calcium phosphate	5.66 mg
Microcrystalline cellulose	15.5 mg
Lactose monohydrate	46.5 mg
Magnesium stearate	0.94 mg

The Agent and crospovidone were blended together for 5 minutes and the blend then passed through a 400–700 um screen. A small portion of the microcrystalline cellulose was passed through the screen afterwards. The screened material was blended with the other ingredients, excluding the lubricant, for 10 minutes. Magnesium stearate was passed through a #40 mesh (425 um) screen and added to the blend and the mixture was blended for a further 3 minutes. The resulting homogeneous mixture was compressed into tablets. The compressed tablets were coated by spraying with a mixture of lactose monohydrate, hydroxypropyl methylcellulose, triacetin and ferric oxide (sold as Opadry II by Colorcon) and water in a coating pan. The weight gain provided by the coating 1 to 6% w/w, and preferably 2 to 3% w/w.

The tablets were stored at 70° C./80% relative humidity for one week. After this time only 0.19% w/w of the oxidation product B2 had formed and only 2.71% w/w of the lactone.

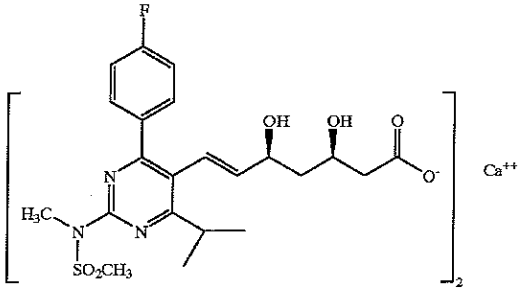
EXAMPLE 4

The Agent	2.50 mg
Povidone	2.50 mg
Tribasic calcium phosphate	20.0 mg
Microcrystalline cellulose	34.5 mg
Lactose monohydrate	34.0 mg
Sodium starch glycollate	6.00 mg
Magnesium stearate	1.00 mg
Butylated hydroxytoluene	0.05 mg

A portion of the tribasic calcium phosphate and butylated hydroxytoluene were blended for 30 seconds in a bag. The Agent, povidone, remainder of the tribasic calcium phosphate, microcrystalline cellulose, lactose monohydrate, tribasic calcium phophate/butylated hydroxytoluene mixture and a portion of the sodium starch glycolate were blended in a granulator for 30 seconds. The powder blend was granulated with purified water for 1 minute at the addition rate of 70 mg/tablet/minute. The granulation is dried in a fluidized bed drier at 50° C. until the loss on drying is less than 2% w/w. The dried granulation is passed through a mill (e.g. Comil). The milled granulation and the remainder of the sodium starch glycolate was blended for approximately 5 minutes. Magnesium stearate was screened through a #40 mesh (425 um) screen and added to the blend and blending continued for a further three minutes. The resulting homogeneous mixture was compressed into tablets.

The tablets were stored at 70° C./80% relative humidity for one week. After this time only 0.23% w/w of the oxidation product B2 had formed and only 0.28% w/w of the lactone. by comparison a similar formulation in which 20.0 mg of tribasic calcium phosphate was replaced by 20.0 mg of dibasic calcium phosphate, 0.19% w/w of B2 was formed and 28.15% w/w of the lactone.

Formula 1



What we claim is:

1. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient and a tribasic phosphate salt in which the cation is multivalent.

2. The pharmaceutical composition as claimed in claim 1 wherein the tribasic phosphate salt in which the cation is multivalent is selected from the group consisting of tribasic calcium phosphate, tribasic magnesium phosphate and tribasic aluminum phosphate.

3. The pharmaceutical composition as claimed in claim 1 or 2 wherein the tribasic phosphate salt in which the cation is multivalent is tribasic calcium phosphate.

4. The pharmaceutical composition as claimed in claim 1 or 2 wherein the ratio of the tribasic phosphate salt to the active ingredient is in the range of 1:80 to 50:1 by weight.

5. The pharmaceutical composition as claimed in claim 1 or 2 additionally comprising one or more fillers, binders, disintegrates or lubricants.

6. A pharmaceutical composition for oral administration comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, one or more fillers, one or more binders, one or more disintegrants, one or more lubricants and a tribasic phosphate salt in which the cation is multivalent.

7. The pharmaceutical composition as claimed in claim 6 wherein the active ingredient is present in an amount 1 to 80% by weight of the composition.

8. The pharmaceutical composition as claimed in claim 6 or 7 wherein the tribasic phosphate salt is present in an amount 1 to 50% by weight of the composition.

9. The pharmaceutical composition as claimed in claim 6 or 7 wherein the filler is present in an amount 30 to 90% by weight of the composition.

10. The pharmaceutical composition as claimed in claim 6 or 7 wherein the binder is present in an amount 2 to 90% by weight of the composition.

11. The pharmaceutical composition as claimed in claim 6 or 7 wherein the disintegrant is present in an amount 2 to 10% by weight of the composition.

12. The pharmaceutical composition as claimed in claim 6 or 7 wherein the lubricant is present in an amount 0.5 to 3% by weight.

13. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, microcrystalline cellulose, lactose, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate.

14. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, microcrystalline cellulose, mannitol, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate.

15. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, crospovidone, microcrystalline cellulose, lactose and magnesium stearate.

16. A pharmaceutical composition comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl) amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof as the active ingredient, tribasic calcium phosphate, povidone, microcrystalline cellulose, lactose, sodium starch glycollate, butylated hydroxytoluene and magnesium stearate.

17. The pharmaceutical composition as claimed in claim 1, 2, 6, 13, 14, 15 or 16 wherein the active ingredient is the calcium salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5- dihydroxyhept-6-enoic acid.

18. A method of producing a stabilised pharmaceutical composition, said method comprising the step of incorporating a tribasic phosphate salt in which the cation is multivalent in a pharmaceutical composition containing the compound (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl (methylsulfonyl)amino]pyrimidin-5-yl]-(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof.

* * * * *

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.

Plaintiff,

v.

Case No.: 8:08-cv-213-T-30TGW

ASTRAZENECA PHARMACEUTICALS LP, et al.

Defendants.

NOTICE OF DESIGNATION UNDER LOCAL RULE 3.05

Please take notice that, in accordance with Local Rule 3.05, this action is designated as a **Track Two** Case. All parties must meet any requirements established in Local Rule 3.05 for cases designated as track two. Counsel and any unrepresented party shall meet within sixty days after service of the complaint upon any defendant for the purpose of preparing and filing a Case Management Report. Parties should utilize the **attached** Case Management Report form. Plaintiff is responsible for serving a copy of this notice and any attachment to this notice upon all other parties.

SHERYL L. LOESCH, CLERK

By: S. Boswell, Deputy Clerk

Date: February 1, 2008

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
Tampa Division

APOTEX INC.

Plaintiff,

v.

Case No.: 8:08-cv-213-T-30TGW

ASTRAZENECA PHARMACEUTICALS LP, et al.

Defendants.

CASE MANAGEMENT REPORT

1. Meeting of Parties: Pursuant to Local Rule 3.05(c)(2)(B) or (c)(3)(A), a meeting was held on _____ (date) at _____ (time) (check one) (__) by telephone (or) (__) at _____ _____ (place) and was attended by:

_____ Name _____ _____ Counsel for (if applicable _____

2. Initial Disclosures:

a. Fed. R. Civ. P. 26(a)(1) as amended December 1, 2000 provides that "[e]xcept in categories of proceedings specified in Rule 26(a)(1)(E), or to the extent otherwise stipulated or directed by order, a party must, without awaiting a discovery request, provide to other parties: (A) the name and, if known, the address and telephone number of each individual likely to have discoverable information that the disclosing party may use to support its claims or defenses, unless solely for impeachment, identifying the subjects of the information; (B) a copy of, or a description by category and location of, all documents, data compilations, and tangible things that are in the possession, custody, or control of the party and that the disclosing party may use to support its claims or defenses, unless solely for impeachment; (C) a computation of any category of damages claimed by the disclosing party, making available for inspection and copying as under Rule 34 the documents or other evidentiary material, not privileged or protected from disclosure, on which such

computation is based, including materials bearing on the nature and extent of injuries suffered; and (D) for inspection and copying as under Rule 34 any insurance agreement under which any person carrying on an insurance business may be liable to satisfy part or all of a judgment which may be entered in the action or to indemnify or reimburse for payments made to satisfy the judgment." Fed. R. Civ. P.26(a)(1).[1]

The parties (check one)

_____ have exchanged information referenced by Fed. R. Civ. P. 26(a)(1)(A)-(D) or agree to exchange such information on or before _____ (date).[2]

_____ stipulate to not disclose information referenced by Fed. R. Civ. P. 26(a)(1)(A)-(D) for the specific reason(s) that:
_____
_____
_____
_____

_____ have been unable to reach agreement on whether to disclose information referenced by Fed. R. Civ. P. 26(a)(1)(A)-(D). (Identify party or parties) _____ objects to disclosure of such information for the specific reason(s) that:
_____
_____
_____
_____

3. Discovery Plan - Plaintiff: The parties jointly propose the following Plaintiff's discovery plan:

a. Plaintiff's Planned Discovery: A description of every discovery effort Plaintiff plans to pursue is described below. The description of each discovery effort will be listed under the appropriate heading below and will include the subject matter of the discovery and the time during which the discovery will be pursued:

[1] A party must make its initial disclosures based on the information then reasonably available to it and is not excused from making its disclosures because it has not fully completed its investigation of the case or because it challenges the sufficiency of another party's disclosures or because another party has not made its disclosures. See Fed. R. Civ. P. 26(a)(1).

[2] Information referenced by Fed. R. Civ. P. 26(a)(1)(A)-(D) must be made "at or within 14 days of the Rule 26(f) conference unless a different time is set by stipulation or court order, or unless a party objects during the conference that initial disclosures are not appropriate in the circumstances of the action and states the objection in the Rule 26(f) discovery plan." Fed. R. Civ. P. 26(a)(1). Any party first served or otherwise joined after the Rule 26(f) conference must make these disclosures within 30 days after being served or joined unless a different time is set by stipulation or court order. See Fed. R. Civ. P. 26(a)(1).

(1) Requests for Admission:

Number of Requests for Admission: Parties may seek to limit the number of Plaintiff's requests for admission in accordance with Fed. R. Civ. P. 26(b)(2). Any such request must be made in paragraph 6 below and approved by the court.

(2) Written Interrogatories:

Number of Interrogatories: Local Rule 3.03(a) provides "[u]nless otherwise permitted by the Court for cause shown, no party shall serve upon any other party, at one time or cumulatively, more than twenty-five (25) written interrogatories pursuant to Rule 33, Fed.R.Civ.P., including all parts and subparts." Any request by Plaintiff to exceed this limit must be made in paragraph 6 below and approved by the court.

(3) Requests for Production or Inspection:

(4) Oral Depositions:

Number of Depositions: Local Rule 3.02(b) provides, "[i]n accordance with Fed. R. Civ. P. 30(a)(2)(A) and 31(a)(2)(A), no more than ten depositions per side may be taken in any case unless otherwise ordered by the Court." Any request by Plaintiff to exceed this limit must be made in paragraph 6 below and approved by the court.

Time Permitted for Each Deposition: Each deposition is limited to one day of seven hours in accordance with Fed. R. Civ. P. 30(d)(2) unless extended by agreement of the parties or order of Court.

The parties stipulate/request a court order to extend the time to take the deposition of the following individuals:

Name	Proposed length of Deposition	Grounds

(cont'd)

Name	Proposed length of Deposition	Grounds

b. Disclosure of Expert Testimony: Parties stipulate, in accordance with Fed. R. Civ. P. 26(a)(2)(C), that Plaintiff's Fed. R. Civ. P. 26(a)(2) disclosure will be due as noted here:

c. Supplementation of Disclosures and Responses: Parties agree that Plaintiff's supplementation under Fed. R. Civ. P. 26(e) will be provided at the following times:

d. Completion of Discovery: Plaintiff will commence all discovery in time for it to be completed on or before _____ (date).

4. Discovery Plan - Defendant: The parties jointly propose the following Defendant's discovery plan:

a. Defendant's Planned Discovery: A description of every discovery effort Defendant plans to pursue is described below. The description of each discovery effort will be listed under the appropriate heading below and will include the subject matter of the discovery and the time during which the discovery will be pursued:

(1) Requests for Admission:

Number of Requests for Admission: Parties may seek to limit the number of Defendant's requests for admission in accordance with Fed. R. Civ. P. 26(b)(2). Any such request must be made in paragraph 6 below and approved by the court.

(2) Written Interrogatories:

Number of Interrogatories: Local Rule 3.03(a) provides "[u]nless otherwise permitted by the Court for cause shown, no party shall serve upon any other party, at one time or cumulatively, more than twenty-five (25) written interrogatories pursuant to Rule 33, Fed.R.Civ.P., including all parts and subparts." Any request by Defendant to exceed this limit must be made in paragraph 6 below and approved by the court.

(3) Requests for Production or Inspection:

(4) Oral Depositions:

Number of Depositions: Local Rule 3.02(b) provides, "[i]n accordance with Fed. R. Civ. P. 30(a)(2)(A) and 31(a)(2)(A), no more than ten depositions per side may be taken in any case unless otherwise ordered by the Court." Any request by Defendant to exceed this limit must be made in paragraph 6 below and approved by the court.

Time Permitted for Each Deposition: Each deposition is limited to one day of seven hours in accordance with Fed. R. Civ. P. 30(d)(2) unless extended by agreement of the parties or order of Court.

The parties stipulate/request a court order to extend the time to take the deposition of the following individuals:

Name	Proposed length of Deposition	Grounds

b. Disclosure of Expert Testimony: Parties stipulate, in accordance with Fed. R. Civ. P. 26(a)(2)(C), that Defendant's Fed. R. Civ. P. 26(a)(2) disclosure will be due as noted here:

c. Supplementation of Disclosures and Responses: Parties agree that Defendant's supplementation under Fed. R. Civ. P. 26(e) will be provided at the following times:

d. Completion of Discovery: Defendant will commence all discovery in time for it to be completed on or before _____ (date).

5. Joint Discovery Plan - Other Matters: Parties agree on the following other matters relating to discovery (*e.g.*, handling of confidential information, assertion of privileges, whether discovery should be conducted in phases or be limited to or focused upon particular issues):

6. Disagreement or Unresolved Issues Concerning Discovery Matters: Any disagreement or unresolved issue will not excuse the establishment of discovery completion dates. The parties are unable to agree as to the following issues concerning discovery:

7. Third Party Claims, Joinder of Parties, Potentially Dispositive Motions: Parties agree that the final date for filing:

a. motions for leave to file third party claims and/or motions to join parties should be _____.

b. motions for summary judgment and all other potentially dispositive motions should be _____. (Note time limit in Local Rule 4.03.)

8. Settlement and Alternative Dispute Resolution: Pursuant to Local Rule 3.05(c)(2)(C)(v), the parties submit the following statement concerning their intent regarding Alternative Dispute Resolution:

Parties agree that settlement is
___ likely (check one)
___ unlikely.

Parties agree to consent to binding arbitration pursuant to Local Rules 8.02(a)(3) and 8.05(b).
_____yes _____no _____likely to agree in future

If binding arbitration is not agreed to, the court may order nonbinding arbitration pursuant to Chapter Eight of the Local Rules of the Middle District of Florida, mediation pursuant to Chapter Nine of the Local Rules of the Middle District of Florida, or both.

9. Consent to Magistrate Judge Jurisdiction: The parties agree to consent to the jurisdiction of the United States Magistrate Judge for final disposition, including trial. See 28 U.S.C. § 636.
_____yes _____no _____likely to agree in future

10. Preliminary Pretrial Conference:
Track Three Cases: Local Rule 3.05(c)(3)(B) provides that preliminary pretrial conferences are mandatory in Track Three Cases.

Track Two Cases: Parties
___request (check one)
___do not request
a preliminary pretrial conference before entry of a Case Management and Scheduling Order in this Track Two case. Unresolved issues to be addressed at such a conference include:

11. Final Pretrial Conference and Trial: Parties agree that they will be ready for a final pretrial conference on or after _____(date) and for trial on or after _____ (date). This **Jury** ___ **Non-Jury** ___ trial is expected to take approximately ____ hours.

12. Pretrial Disclosures and Final Pretrial Procedures: Parties acknowledge that they are aware of and will comply with pretrial disclosures requirements in Fed. R. Civ. P. 26(a)(3) and final pretrial procedures requirements in Local Rule 3.06.

13. Other Matters:

Date: _____

Signature of Counsel (with information required by Local Rule 1.05(d)) and
Signature of Unrepresented Parties

_____

_____

_____

_____

_____

_____

_____

AO85A (Rev. 8/98) Consent to Exercise of Jurisdiction by a United States Judge Over Specific Motion(s)

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

_____

_____

v. **Case No.**

_____

_____

CONSENT TO EXERCISE JURISDICTION BY A UNITED STATES MAGISTRATE JUDGE OVER DISPOSITIVE MOTIONS DESCRIBED UNDER 28 U.S.C. § 636(b)(1)(B)

CONSENT TO EXERCISE OF JURISDICTION

In accordance with the provisions of 28 U.S.C. § 636(c) and Fed.R.Civ.P. 73, the parties in this case consent to have a United States Magistrate Judge conduct any and all proceedings and enter a final order as to each motion identified below.

MOTION(S) _____

_____

_____

Party Represented	Signatures	Date
_____	_____	_____
_____	_____	_____
_____	_____	_____

ORDER OF REFERENCE

IT IS ORDERED that the above motions(s) be referred to the United States Magistrate Judge assigned to this case to conduct all proceedings and enter a final order on such motions(s) in accordance with 28 U.S.C. § 636(c) and Fed.R.Civ.P. 73.

_____ _____

Date United States District Judge

NOTE: RETURN THIS FORM TO THE CLERK OF COURT **ONLY IF** ALL PARTIES HAVE CONSENTED **ON THIS FORM** TO THE EXERCISE OF JURISDICTION BY A UNITED STATES MAGISTRATE JUDGE.

UNITED STATES DISTRICT COURT

Middle District of Florida

Plaintiff
V.

Defendant

NOTICE, CONSENT, AND ORDER OF REFERENCE — EXERCISE OF JURISDICTION BY A UNITED STATES MAGISTRATE JUDGE

Case Number:

NOTICE OF AVAILABILITY OF A UNITED STATES MAGISTRATE JUDGE TO EXERCISE JURISDICTION

In accordance with the provisions of 28 U.S.C. §636(c), and Fed.R.Civ.P. 73, you are notified that a United States magistrate judge of this district court is available to conduct any or all proceedings in this case including a jury or nonjury trial, and to order the entry of a final judgment. Exercise of this jurisdiction by a magistrate judge is, however, permitted only if all parties voluntarily consent.

You may, without adverse substantive consequences, withhold your consent, but this will prevent the court's jurisdiction from being exercised by a magistrate judge. If any party withholds consent, the identity of the parties consenting or withholding consent will not be communicated to any magistrate judge or to the district judge to whom the case has been assigned.

An appeal from a judgment entered by a magistrate judge shall be taken directly to the United States court of appeals for this judicial circuit in the same manner as an appeal from any other judgment of this district court.

CONSENT TO THE EXERCISE OF JURISDICTION BY A UNITED STATES MAGISTRATE JUDGE

In accordance with provisions of 28 U.S.C. §636(c) and Fed.R.Civ.P. 73, the parties in this case consent to have a United States magistrate judge conduct any and all proceedings in this case, including the trial, order the entry of a final judgment, and conduct all post-judgment proceedings.

Party Represented	Signatures	Date

ORDER OF REFERENCE

IT IS ORDERED that this case be referred to _____ United States Magistrate Judge, to conduct all proceedings and order the entry of judgment in accordance with 28 U.S.C. §636(c) and Fed.R.Civ.P. 73.

Date

United States District Judge

NOTE: RETURN THIS FORM TO THE CLERK OF THE COURT ONLY IF ALL PARTIES HAVE CONSENTED ON THIS FORM TO THE EXERCISE OF JURISDICTION BY A UNITED STATES MAGISTRATE JUDGE.

AO 440 (Rev. 8/01) Summons in a Civil Action

UNITED STATES DISTRICT COURT

MIDDLE District of FLORIDA

APOTEX INC.

v.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.

SUMMONS IN A CIVIL CASE

CASE NO: 8:08-cv-00213-JSM-TGW

TO: (Name and address of Defendant)

ASTRAZENECA PHARMACEUTICALS LP
c/o CT Corporation System, Registered Agent
1200 South Pine Island Road
Plantation, FL 33324

YOU ARE HEREBY SUMMONED and required to serve on PLAINTIFF'S ATTORNEY (name and address)

Lee Fugate
Zuckerman Spaeder LLP
101 E. Kennedy Blvd., Suite 1200
Tampa, FL 33602
Ph: 813-221-1010; Fax: 813-223-7961

an answer to the complaint which is served on you with this summons, within 20 days after service of this summons on you, exclusive of the day of service. If you fail to do so, judgment by default will be taken against you for the relief demanded in the complaint. Any answer that you serve on the parties to this action must be filed with the Clerk of this Court within a reasonable period of time after service.

SHERYL L. LOESCH
CLERK

Denise L. Vought
(By) DEPUTY CLERK

02/06/08
DATE

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v. Case No.: 8:08-cv-213-JSM-TGW

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.
_____/

AGREED MOTION FOR ENLARGEMENT OF TIME

Defendants, ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC., through undersigned counsel, move this Court to enter an Order enlarging the time within which they must respond to Plaintiff's Complaint, through and including March 26, 2008, and as grounds therefor state:

1. Absent an enlargement of time, Defendants' response to Plaintiff's Complaint is due on February 25, 2008.

2. As a result of on-going discussions between counsel for the parties, Defendants respectfully request that the time within which they be required to respond to Plaintiff's Complaint be enlarged by thirty (30) days.

LOCAL RULE 3.01(g) CERTIFICATION

The undersigned certifies that counsel for Defendants has conferred with Plaintiff's counsel, and that Plaintiff's counsel has no objection to the granting of the relief requested herein.

WHEREFORE, Defendants respectfully request this Court enter an Order enlarging the time within which they must respond to Plaintiff's Complaint, through and including March 26, 2008.

Respectfully submitted,

s/William C. Guerrant, Jr.
William C. Guerrant, Jr.
Florida Bar No. 516058
Attorneys for Defendants
HILL, WARD & HENDERSON, P.A.
Suite 3700 – Bank of America Building
101 East Kennedy Boulevard
Post Office Box 2231
Tampa, Florida 33601
Telephone: (813) 221-3900
Facsimile: (813) 221-2900
E-mail: wguerrant@hwhlaw.com

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on February 8, 2008, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to Lee Fugate and Nathan M. Berman, Zuckerman Spaeder LLP, 101 E. Kennedy Boulevard, Suite 1200, Tampa, Florida 33602 and to Robert B. Breisblatt, J. Aron Carnahan and Laurie A. Haynie, Welsh & Katz, Ltd., 120 S. Riverside Plaza, 22nd Floor, Chicago, Illinois 60606.

s/William C. Guerrant, Jr.
Attorney

127956

AO 440 (Rev. 8/01) Summons in a Civil Action

UNITED STATES DISTRICT COURT

MIDDLE District of FLORIDA

APOTEX INC.

SUMMONS IN A CIVIL CASE

V.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.

CASE NO: 8:08-cv-00213-JSM-TGW

TO: (Name and address of Defendant)

IPR PHARMACEUTICALS, INC.
c/o
Carr 188 Lote 17
San Isidro Industrial Park
Canovanas, Puerto Rico 00729

YOU ARE HEREBY SUMMONED and required to serve on PLAINTIFF'S ATTORNEY (name and address)

Lee Fugate
Zuckerman Spaeder LLP
101 E. Kennedy Blvd., Suite 1200
Tampa, FL 33602
Ph: 813-221-1010; Fax: 813-223-7961

an answer to the complaint which is served on you with this summons, within 20 days after service of this summons on you, exclusive of the day of service. If you fail to do so, judgment by default will be taken against you for the relief demanded in the complaint. Any answer that you serve on the parties to this action must be filed with the Clerk of this Court within a reasonable period of time after service.

SHERYL L. LOESCH

CLERK

Liz Vasquez

(By) DEPUTY CLERK

02/06/08 FEB 08 2008

DATE

AO 440 (Rev. 8/01) Summons in a Civil Action

UNITED STATES DISTRICT COURT

MIDDLE District of FLORIDA

APOTEX INC.

SUMMONS IN A CIVIL CASE

V.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.

CASE NO: 8:08-cv-00213-JSM-TGW

TO: (Name and address of Defendant)

ASTRAZENECA UK LIMITED
c/o
15 Stanhope Gate
London, W1K 1LN, England

YOU ARE HEREBY SUMMONED and required to serve on PLAINTIFF'S ATTORNEY (name and address)

Lee Fugate
Zuckerman Spaeder LLP
101 E. Kennedy Blvd., Suite 1200
Tampa, FL 33602
Ph: 813-221-1010; Fax: 813-223-7961

an answer to the complaint which is served on you with this summons, within 20 days after service of this summons on you, exclusive of the day of service. If you fail to do so, judgment by default will be taken against you for the relief demanded in the complaint. Any answer that you serve on the parties to this action must be filed with the Clerk of this Court within a reasonable period of time after service.

SHERYL L. LOESCH

CLERK

(By) DEPUTY CLERK

FEB 0 8 2008

02/08/08

DATE

VERIFIED RETURN OF SERVICE

Insert name of court, judicial district or branch court, if any:	
United States District Court, Middle District of Florida	
DEPOSITION/COURT DATE:	CASE NUMBER: 8:08-cv-00213-JSM-TGW
PLAINTIFF/PETITIONER: Apotex, Inc.	
DEFENDANT/RESPONDENT: Astrazeneca Pharmaceuticals, LP, et al	
DOCUMENTS SERVED: 20 Day Summons, Complaint for Declaratory Relief with Exhibits	

Received on **02/11/2008** at **3:38 PM** to be served on:

Astrazeneca Pharmaceuticals, LP c/o CT Corp. - RA

I do hereby affirm that on **02/13/2008** at **9:00 AM** I served this process by:

XXX CORPORATE SERVICE: By leaving a true copy of this process with the date and hour of service endorsed thereon by me, a copy of the complaint, petition, or other initial pleading or paper (if any) and informing the person of the contents:

NAME: **CT Corp** TITLE: **Registered Agent**

___ OTHER: By delivering a true copy of this process to _____, _____ and informing him/her of the contents.

___ NON-SERVICE: For the reason(s) listed in the comments below:

LOCATION OF SERVICE:	FOR(Client):
1200 South Pine Island Road Plantation, FL 33324	Lee Fugate, Esq. Zuckerman Spaeder, LLP 101 East Kennedy Boulevard, Suite 1200 Tampa, FL 33602 813-221-1010

COMMENTS:

AUTHORIZATION:

I AM APPOINTED IN GOOD STANDING IN THE JUDICIAL CIRCUIT WHEREIN THIS PROCESS WAS SERVED AND HAVE NO INTEREST IN THE ABOVE ACTION.

DECLARATION:	SIGNATURE:
UNDER PENALTIES OF PERJURY I DECLARE THAT I HAVE READ THE FOREGOING VERIFIED RETURN OF SERVICE AND THAT THE FACTS STATED IN IT ARE TRUE. NOTARY NOT REQUIRED PURSUANT TO F.S. 92.525(2).	X_____ Jack Lippman - Cert/Appt#: 284-Broward County State Service Corporation 4030 Powerline Rd. Ft. Lauderdale, FL 33309 OUR FILE#: **95121**

AO 440 (Rev. 8/01) Summons in a Civil Action

UNITED STATES DISTRICT COURT

MIDDLE District of FLORIDA

APOTEX INC.

SUMMONS IN A CIVIL CASE

V.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.

CASE NO: 8:08-cv-00213-JSM-TGW

TO: (Name and address of Defendant)

ASTRAZENECA PHARMACEUTICALS LP
c/o CT Corporation System, Registered Agent
1200 South Pine Island Road
Plantation, FL 33324

STATE SERVICE

YOU ARE HEREBY SUMMONED and required to serve on PLAINTIFF'S ATTORNEY (name and address)

Lee Fugate
Zuckerman Spaeder LLP
101 E. Kennedy Blvd., Suite 1200
Tampa, FL 33602
Ph: 813-221-1010; Fax: 813-223-7961

an answer to the complaint which is served on you with this summons, within 20 days after service of this summons on you, exclusive of the day of service. If you fail to do so, judgment by default will be taken against you for the relief demanded in the complaint. Any answer that you serve on the parties to this action must be filed with the Clerk of this Court within a reasonable period of time after service.

SHERYL L. LOESCH
CLERK

02/06/08
DATE

(By) DEPUTY CLERK

STATE SERVICE
95121

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v. Case No.: 8:08-cv-213-JSM-TGW

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.
_____/

UNOPPOSED MOTION FOR ENLARGEMENT OF TIME

Defendants, ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC., move this Court to enter an order enlarging the time within which they must respond to Plaintiff's Complaint, through and including April 9, 2008, and as grounds therefor state:

1. Absent an enlargement of time, the response to Plaintiff's Complaint is due on March 26, 2008.

2. Developments in the case make it necessary for Defendants to request an additional 14 days within which to submit their response, and counsel for Plaintiff has indicated that it has no objection to the granting of such an enlargement of time.

LOCAL RULE 3.01(g) CERTIFICATION

Counsel for Defendants have conferred with counsel for Plaintiff, and counsel for Plaintiff has no objection to the granting of the relief requested herein.

WHEREFORE, Defendants respectfully request this Court enter an order enlarging the time within which they must respond to Plaintiff's Complaint, through and including April 9, 2008.

Respectfully submitted,

s/William C. Guerrant, Jr.
William C. Guerrant, Jr.
Florida Bar No. 516058
Attorneys for Defendants
HILL, WARD & HENDERSON, P.A.
Suite 3700 – Bank of America Building
101 East Kennedy Boulevard
Post Office Box 2231
Tampa, Florida 33601
Telephone: (813) 221-3900
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E-mail: wguerrant@hwhlaw.com

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on March 26, 2008, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to Lee Fugate and Nathan M. Berman, Zuckerman Spaeder LLP, 101 E. Kennedy Boulevard, Suite 1200, Tampa, Florida 33602 and to Robert B. Breisblatt, J. Aron Carnahan and Laurie A. Haynie, Welsh & Katz, Ltd., 120 S. Riverside Plaza, 22nd Floor, Chicago, Illinois 60606.

s/William C. Guerrant, Jr.
Attorney

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v.

CASE NO. 8:08-cv-00213-T-30TGW

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.

_____/

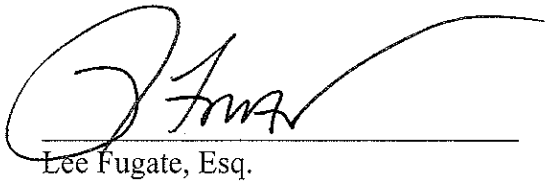
NOTICE OF CHANGE OF ADDRESS

PLEASE TAKE NOTICE that the undersigned, who are co-counsel for the Plaintiff, APOTEX, INC., in the above-referenced matter, has relocated his law office. The updated contact information is as follows:

Robert B. Breisblatt, Esq.
Katten Muchin Rosenman LLP
525 West Monroe Street
Chicago, Illinois 60661-3693
Tel: (312) 902-5480
E-Mail: Robert.breisblatt@kattenlaw.com

Dated: April 1, 2008

Respectfully submitted,



Lee Fugate, Esq.
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Ph: 813.221.1010
Fax: 813.223-7961

CERTIFICATE OF SERVICE

I hereby certify that on April 1, 2008, I served upon opposing counsel, via electronic mail, Plaintiff's Notice of Address Change with the Clerk of the Court using the CM/ECF system which will automatically send email notification of such filing to the following attorneys of record:

William C. Guerrant, Jr., Esq.
HILL, WARD & HENDERSON, P.A.
Suite 3700 – Bank of America Building
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Post Office Box 2231
Tampa, Florida 33601

J. Aron Carnahan, Esq.
Laurie A. Haynie, Esq.
Welsh & Katz, Ltd.
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Robert B. Breisblatt, Esq.
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525 West Monroe Street
Chicago, Illinois 60661-3693

Lee Fugate, Esq.

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.

Civil Action No.: 8:08-cv-213-JSM-TGW

DEFENDANTS' MOTION FOR LEAVE TO FILE UNDER SEAL
AND MEMORANDUM OF LAW IN SUPPORT THEREOF

Pursuant to Middle District of Florida Local Rule 1.09, Defendants request leave to file under seal certain portions of their Motion to Dismiss and Memorandum of Law in Support Thereof and to file under seal a certain non-public written communication with Apotex Inc. and Apotex Corp. (collectively, "Apotex") that will be exhibited in support of Defendants' motion to dismiss. The communication eliminates any case or controversy between the parties concerning U.S. Patent No. 6,316,460 ("the '460 patent").

I. PROCEDURAL BACKGROUND

Defendants in this case sued Apotex on December 11, 2007, in the U.S. District Court of Delaware for infringement of U.S. Reissue Patent RE37,314 ("the '314 patent"), which claims the active ingredient, rosuvastatin calcium, in AstraZeneca's highly successful drug CRESTOR®. The action resulted from Apotex's filing Abbreviated New Drug Application ("ANDA") No. 79-145 with the United States Food and Drug Administration ("FDA"), and

certification to the FDA that it intends to market generic versions of CRESTOR® before the '460 and '314 patents expire.[1] Defendants, however, did not sue Apotex on the '460 patent. Rather than respond to the Delaware Complaint, Apotex contested jurisdiction there and filed its own Complaint here in the Middle District of Florida, raising only a declaratory judgment claim against the '460 patent.

Since then, Defendants have communicated with Apotex in writing regarding the '460 patent. The communication eliminates any case or controversy regarding that patent. As a result of that non-public communication, Defendants plan to file a motion to dismiss this action. Defendants intend to attach the writing as an exhibit to their motion. The communication contains Defendants' confidential business information, which would commercially benefit other parties opposing Defendants in other litigations. To protect that confidential information, Defendants seek leave to file the following documents under seal: 1) the portions of the motion to dismiss discussing the non-public communication, and 2) the communication.

II. LEGAL AUTHORITY AND REASONS FOR FILING UNDER SEAL

According to Moore's Federal Practice:

> 'Every court has supervisory power over its own records and files, and access has been denied where the court files might have become a vehicle for improper purposes.' Courts have always possessed the general power to restrict access to judicial

[1] Apotex is among seven generic pharmaceutical companies to so challenge the '314 patent. In an effort to resolve the multiple challenges to its patent rights, Defendants filed seven related patent infringement actions in the District of Delaware on December 11, 2007 (C.A. Nos. 07-805, 07-806, 07-807, 07-808, 07-809, 07-810, and 07-811). Defendants have also filed a motion with the Judicial Panel on Multidistrict Litigation to transfer this and a similar, now stayed, action in New Jersey to Delaware for coordinated pretrial proceedings.

> records, including obviously sensitive and confidential information. … A party may request a court to restrict public access to filed papers on a showing that the disclosure would be harmful. In response to this type of request, a court will weigh the competing private and public interests and determine, under a balancing test, whether the private interests furthered by denying public access, *e.g.,* preventing unfair pretrial publicity … or protecting privacy interests, outweigh the public's interest to inspect judicial records.

1 Jeremy C. Moore *et al.,* Moore's Federal Practice ¶ 5.34[2][c] (3d ed. 2008) (citing *Nixon v. Warner Communications, Inc.,* 435 U.S. 589 (1978)).

To avoid harming Defendants' future dealings with similarly situated adversaries and misperceptions that may arise from disclosure,[2] Defendants request that the non-public communication and the portions of their forthcoming motion to dismiss discussing the communication not be made available to the public.[3] There is no resulting prejudice to either Apotex or the public by filing that information under seal. Apotex will have full access to both the motion and the exhibited writing. In other words, Defendants propose to file with the Court and serve upon Plaintiff complete copies of the motion and communication under seal, while simultaneously providing the Court with a public version of the motion, without the

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[2] False impressions have already arisen in this context when the publication IPLaw360, misrepresented certain aspects of this litigation, including stating that the underlying '460 patent was "already at the center of myriad complaints that AstraZeneca has fired off in recent months against Apotex and a number of other generics makers …." Sarah Stefanini, Generic Won't Infringe Crestor Patent, Apotex Claims, IPLaw360, February 1, 2008 (available at http://ip.law360.com/Secure/ViewArticle.aspx?id=45921). In reality, AstraZeneca has never asserted that patent against any party in any litigation.

[3] The communications, despite their dispositive effect on this action, are not a settlement agreement. (*Cf.* Local Rule 1.09 ("No settlement agreement shall be sealed absent extraordinary circumstances … .").)

exhibit, containing redactions over the portions that discuss the non-public exhibited communication.

Because public disclosure at this early stage of the proceeding can only harm Defendants with no concomitant benefit to Apotex or the public, Defendants respectfully request that the Court seal the communication and those portions of Defendants' motion to dismiss discussing the communication for one year, as provided under the Local Rule.

Local Rule 3.01(g) Certification

The undersigned certifies that counsel for Defendants has conferred with counsel for Plaintiff, but was unable to reach agreement regarding this Motion.

Dated: April 1, 2008

Respectfully submitted,

s/Lara J. Tibbals
William C. Guerrant, Jr.
Florida Bar No. 516058
Lara J. Tibbals
Florida Bar No. 129054
Attorneys for Defendants
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E-mail: ltibbals@hwhlaw.com

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on April 1, 2008, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to Lee Fugate and Nathan M. Berman, Zuckerman Spaeder LLP, 101 E. Kennedy Boulevard, Suite 1200, Tampa, Florida 33602 and to Robert B. Breisblatt, J. Aron Carnahan

and Laurie A. Haynie, Welsh & Katz, Ltd., 120 S. Riverside Plaza, 22nd Floor, Chicago, Illinois 60606.

s/Lara J. Tibbals
Attorney

485200

IN THE UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.

Civil Action No.: 8:08-cv-213-JSM-TGW

DEFENDANTS' NOTICE OF WITHDRAWAL OF MOTION FOR LEAVE TO FILE UNDER SEAL

Defendants hereby withdraw their Motion for Leave to File Under Seal (Dkt. #13) from the Court's consideration.

Dated: April 9, 2008

Respectfully submitted,

s/Lara J. Tibbals
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Florida Bar No. 516058
Lara J. Tibbals
Florida Bar No. 129054
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s/Lara J. Tibbals
Attorney

496416

IN THE UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.

Civil Action No.: 8:08-cv-213-JSM-TGW

DISPOSITIVE MOTION

DEFENDANTS' MOTION TO DISMISS COMPLAINT WITH PREJUDICE AND SUPPORTING MEMORANDUM OF LAW

Defendants AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, and IPR Pharmaceuticals, Inc. (collectively "AstraZeneca") hereby move to dismiss Apotex Inc.'s Complaint with prejudice for lack of subject matter jurisdiction pursuant to Fed. R. Civ. P. 12(b)(1).

I. THE NATURE AND STAGE OF THE PROCEEDING

Apotex Inc. ("Apotex") has sued AstraZeneca for a declaratory judgment of non-infringement of U.S. Patent No. 6,316,460 ("the '460 patent"). That patent claims a drug formulation for AstraZeneca's highly successful, cholesterol-lowering drug, CRESTOR®. This action results from Apotex filing Abbreviated New Drug Application ("ANDA") No. 79-145 with the United States Food and Drug Administration ("FDA") and certifying that it intends to market generic versions of AstraZeneca's CRESTOR® products before expiration

of the '460 patent and U.S. Reissue Patent RE37,314 ("the '314 patent"), a related patent that covers CRESTOR®'s active ingredient, rosuvastatin calcium.

Apotex is one of seven generic drug manufacturers to so challenge the '314 and '460 patents. In an effort to resolve the multiple challenges to its patent rights, AstraZeneca filed seven related patent infringement actions in the District of Delaware on December 11, 2007.[1] The Complaint in each action alleges infringement of only the '314 patent. Rather than answer the Complaint, Apotex moved to dismiss the Delaware action for lack of jurisdiction and simultaneously initiated this action in the Middle District of Florida. Significantly, Apotex's declaratory judgment action only involves the '460 patent. Because AstraZeneca has given Apotex a covenant not to sue under the '460 patent, AstraZeneca seeks to dismiss Apotex's Complaint with prejudice.

II. SUMMARY OF ARGUMENT

AstraZeneca gave Apotex a covenant not to sue under the '460 patent. As federal courts have repeatedly held, a covenant not to sue divests the court of subject matter jurisdiction, renders moot the declaratory judgment claim regarding patent infringement and validity, and eliminates any alleged Article III standing relating to the patent claim.

III. STATEMENT OF FACTS

This case concerns AstraZeneca's CRESTOR® pharmaceutical product, and Apotex's efforts to sell a generic version of CRESTOR® before the '460 patent expires. On November 5, 2007, Apotex notified AstraZeneca of its ANDA No. 79-145, seeking FDA approval to

[1] Civil Action Nos. 07-805, 07-806, 07-807, 07-808, 07-809, 07-810, and 07-811. Apotex Inc. and its U.S. subsidiary, Apotex Corp., are defendants in Civil Action 07-809.

engage in the manufacture, importation, use or sale of generic rosuvastatin calcium before the '460 patent expires. Subsequently, on December 4, 2007, Apotex notified AstraZeneca that it had amended the ANDA, certifying its intention to sell generic rosuvastatin calcium before expiration of the '314 patent, as well. In response, AstraZeneca filed suit against Apotex and its subsidiary, Apotex Corp., in the District of Delaware, but only on the '314 patent.

Apotex moved to dismiss AstraZeneca's Delaware complaint and simultaneously filed this action, seeking a declaratory judgment that its proposed generic rosuvastatin calcium product will not infringe the '460 patent. (Dkt. #1, ¶¶ 21-23.) On March 25, 2008, AstraZeneca gave Apotex a covenant not to sue on the '460 patent. (Ex. A.) Because the covenant not to sue eliminates any potential case or controversy related to the '460 patent, AstraZeneca now moves to dismiss Apotex's Complaint with prejudice for lack of subject matter jurisdiction pursuant to Fed. R. Civ. P. 12(b)(1).

IV. ARGUMENT

To establish jurisdiction under the Declaratory Judgment Act, Apotex bears the burden of proving that the facts alleged "under all the circumstances show that there is a substantial controversy, between the parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *MedImmune, Inc. v. Genentech, Inc.*, 127 S. Ct. 764, 771 (2007). Under this standard, AstraZeneca's covenant not to sue Apotex for infringement of the '460 patent dictates dismissal of all the claims in Apotex's Complaint for at least three reasons. First, it divests this Court of subject matter jurisdiction over Apotex's Complaint, because it conclusively resolves any potential case or controversy. Second, without a case or controversy, Apotex's claims become hypothetical, advisory, and, thus, improper. Third, the covenant eliminates any Article III standing, because Apotex

cannot identify any requisite injury in fact. *See Pfizer, Inc. v. Ranbaxy Labs. Ltd,* 525 F. Supp. 2d 680, 684 (D. Del. Nov. 29, 2007); *Merck & Co., Inc. v. Apotex, Inc.,* 488 F. Supp. 2d 418, 424 (D. Del. May 21, 2007) (Apotex counterclaim dismissed because, "it is well-established that a trial court may be divested or deprived of subject matter jurisdiction over a particular patent claim if the patentee covenants not to assert an infringement claim against a putative infringer."); *Janssen Pharmaceuticals, N.V. v. Apotex, Inc.,* 2007 WL 3014702, at *2 (D.N.J. October 11, 2007) (Apotex counterclaims dismissed, "because there is no case or controversy surrounding the patents Defendant alleges are in issue" where covenant not to sue was given.).

In both *Janssen* and *Merck*, Apotex opposed motions to dismiss its declaratory judgment counterclaims, asserting that the Federal Circuit's recent decision in *Teva Pharms. USA, Inc. v. Novartis Pharms. Corp.,* 482 F.3d 1330 (Fed. Cir. 2007) prevented dismissal. Both courts, however, ruled against Apotex because, unlike the situation in *Novartis*, the patentees in *Janssen* and *Merck*, as here, had given Apotex a covenant not to sue. *Janssen*, 2007 WL 3014702, at *3 ("the present action is distinguished from *Novartis* as [patentee] point[s] out, there was no covenant not to sue in *Novartis*." (citation omitted)); *Merck*, 488 F. Supp. 2d at 423 ("A significant distinction between the scenario in *Teva v. Novartis* and the case here is that Novartis had declined to give Teva a covenant not to sue."). Indeed, the *Janssen* court relied on *Novartis* to rule that "a covenant not to sue usurps the opportunity to bring an action for declaratory judgment." *Janssen,* 2007 WL 3014702 at *3.

In another recent case, the patentee had brought suit against a generic drug manufacturer on two patents. *Pfizer v. Ranbaxy,* 525 F. Supp. 2d 680, 683-684. In response,

the generic drug manufacturer filed, *inter alia*, counterclaims seeking declaratory relief on a third patent that the patentee had not asserted and on which the patentee had given a covenant not to sue. Similar to the situation here, the patentee "contend[ed] that there [was] no justiciable case or controversy between the parties and no declaratory judgment jurisdiction with respect to these counterclaims based on the covenant not to sue." *Id.* at 685. The court agreed, ruling that a covenant not to sue conclusively divested the court of subject matter jurisdiction. *Id.* at 686 (citing *Merck,* 488 F. Supp. at 423-425); *see also id.* at 687 (advisory opinions are "wholly inconsistent with the most basic precepts of jurisdictional jurisprudence."). The court also held that the covenant not to sue removed any Article III standing, because the Defendant had not suffered any requisite injury in fact. *Id.*

The recent decision by the Federal Circuit in *Caraco Pharm. Labs., Ltd. v. Forest Labs., Inc.,* 2008 U.S. App. LEXIS 6383 (Fed. Cir. April 1, 2008), should not affect the outcome of this motion, because it is both legally and factually inapposite to the current dispute. First, and most importantly, the ANDA filer in *Caraco* was not the first ANDA filer, which in that case acted as an impediment to market entry of its generic product. In the present case, Apotex is considered a first filer,[2] thereby freeing it of the restraints on market entry identified in the *Caraco* decision.[3]

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[2] AstraZeneca has reason to believe that Apotex Inc. and Apotex Corp. are considered first-filers, because under the rules, every party that files a substantially complete ANDA on the first day allowed under law is considered a first filer. *See* 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb).

[3] The *Caraco* decision was grand-fathered into and thus governed by old Hatch-Waxman rules, which, in part, tied market entry for subsequent ANDA filers to the first filer's market entry. Amendments to the Hatch-Waxman Act in 2003, which govern this case, have resolved this issue by including safeguards for subsequent ANDA filers, thereby rendering the

(continued on next page)

Under the regulatory scheme created by the Hatch Waxman Act, generic drug manufacturers are given incentives to challenge patents covering branded drug products. One of those incentives is the granting of a 180-day period of market exclusivity for the first generic drug manufacturer to file an ANDA. Subsequent ANDA filers must wait until the first filer's 180-day exclusivity period ends before entering the market. According to the Federal Circuit's interpretation of the old rules in *Caraco*, the 180-day period is "triggered" when either the first filer enters the marketplace or any filer obtains a judgment successfully challenging the relevant Orange Book listed patents. *Id.* at 5. The Court also interpreted the old rules to allow for second filers to trigger the 180-day period by obtaining a judgment that all of the Orange Book listed patents are invalid, unenforceable, or not infringed. *Id.* at 6-7.

In *Caraco*, the first ANDA filer was held to infringe one of the Orange Book listed patents at issue. As a result, it was precluded from entering the market and triggering the 180-day exclusivity period. Additionally, the patent owner gave the subsequent ANDA filer a covenant not to sue on the second of only two Orange Book listed patents, preventing the second filer from obtaining a judgment on all of the Orange Book listed patents. Under those circumstances, the Federal Circuit ruled that the covenant not to sue did not eliminate the case or controversy on the patents, because the second ANDA filer was in fact injured—it could not enter the market because the first ANDA filer could not trigger the 180-day exclusivity

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(continued from previous page)
ANDA filer's predicament in *Caraco* altogether moot. *See* 21 U.S.C. § 355(j)(5)(D). As the Court explained in *Caraco*, "the…amendments to the provisions governing the commencement of 180-day exclusivity period are inapplicable to this case." *Caraco,* 2008 U.S. App. LEXIS at n.2.

period, and without the ability to obtain a judgment on both patents, the second ANDA filer could not independently trigger that exclusivity period.

Here, there is no such injury-in-fact. The covenant at issue will not prevent Apotex, a first filer, from entering the market. If anything, it removes a potential barrier from Apotex's market entry if Apotex is successful in challenging the '314 patent in the Delaware action. Accordingly, the *Caraco* decision does not apply here, and AstraZeneca's covenant not to sue eliminates the case or controversy over the '460 patent.

Just as the covenants not to sue in similar situations were dispositive of the *Janssen, Merck*, and *Pfizer* cases, the covenant not to sue that AstraZeneca gave Apotex is dispositive of this case. As a result of the covenant, the Court is divested of subject matter jurisdiction over Apotex's declaratory judgment action, Apotex's declaratory judgment claim is rendered moot, and Apotex lacks standing to maintain this suit.

V. CONCLUSION

For the forgoing reasons, AstraZeneca respectfully requests that the Court dismiss Apotex's Complaint with prejudice for lack of subject matter jurisdiction under Fed. R. Civ. P. 12(b)(1).

Dated: April 10, 2008

Respectfully submitted,

s/Lara J. Tibbals
William C. Guerrant, Jr., FBN 516058
Lara J. Tibbals, FBN 129054
Attorneys for Defendants
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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on April 10, 2008, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to Lee Fugate and Nathan M. Berman, Zuckerman Spaeder LLP, 101 E. Kennedy Boulevard, Suite 1200, Tampa, Florida 33602 and to Robert B. Breisblatt, J. Aron Carnahan and Laurie A. Haynie, Welsh & Katz, Ltd., 120 S. Riverside Plaza, 22nd Floor, Chicago, Illinois 60606.

s/Lara J. Tibbals
Attorney

FINNEGAN HENDERSON FARABOW GARRETT & DUNNER LLP

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March 25, 2008

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Zuckerman Spaeder LLP
101 E. Kennedy Boulevard
Suite 1200
Tampa, FL. 33602

Via E-Mail

Apotex v. AstraZeneca, C.A No. 8:08-cv-213-JSM-TGW

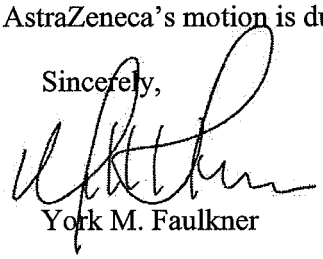
Dear Counsel:

We write regarding the above-referenced action that Apotex, Inc. filed in the Middle District of Florida, seeking declaratory relief that the product described in ANDA No. 79-145 does not infringe U.S. Patent No. 6,316,460 (the '460 patent). AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals, Inc., and AstraZeneca AB (collectively "AstraZeneca") covenant not to assert infringement of the '460 patent on the following conditions. Specifically, provided that the formulation of the proposed product as described in the excerpts given to AstraZeneca from ANDA No. 79-145 does not change, AstraZeneca represents that it will not sue Apotex Inc. or Apotex Corp. for any infringement of any claim of the '460 patent concerning the rosuvastatin calcium product for which ANDA No. 79-145 currently seeks FDA approval.

Exhibit "A"

This commitment eliminates any case or controversy alleged in C.A No. 8:08-cv-213. Accordingly, AstraZeneca will move to dismiss Apotex's Inc.'s Complaint for Declaratory Relief rather than answer it. Nevertheless, we prefer to avoid unnecessary motion practice and are open to discussing this further with the objective of obtaining consent to the dismissal of this action before Apotex Inc.'s opposition to AstraZeneca's motion is due.

Sincerely,



York M. Faulkner

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v.

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.

Civil Action No.: 8:08-cv-213-JSM-TGW

DEFENDANTS' MOTION FOR A TEMPORARY STAY
AND MEMORANDUM OF LAW IN SUPPORT THEREOF

I. INTRODUCTION

Defendants, AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, and IPR Pharmaceuticals, Inc. (collectively "AstraZeneca"), seek a temporary stay of this patent action, pending a decision by the Judicial Panel on Multidistrict Litigation ("JPMDL") on AstraZeneca's motion to transfer this and a related action to Delaware for coordinated pretrial proceedings. This is one of nine related cases involving the same drug product, seven of which are pending in Delaware and one in New Jersey. Among the Delaware actions is AstraZeneca's action against the Plaintiff here, Apotex Inc., and its subsidiary, Apotex Corp., and two of the Delaware actions involve the same patent at issue here, U.S. Patent No. 6,316,460 ("the '460 patent"). The court in New Jersey already *sua sponte* stayed the one New Jersey action, pending decision by the JPMDL, as AstraZeneca now asks this Court to do.

Apotex Inc. will not be materially prejudiced by the temporary stay, because it will be participating in discovery in Delaware, which can be used here if necessary. Staying this action until the JPMDL decision, however, will avoid unnecessary duplication of efforts, if this action is transferred by the JPMDL to Delaware for coordinated pretrial proceedings.

Although AstraZeneca recently moved to dismiss this action, Apotex Inc. has indicated that it intends to oppose that motion, thereby prolonging the case. Accordingly, the Court should stay this action until the JPMDL resolves AstraZeneca's motion to transfer the case to Delaware, where two cases involving the '460 patent are pending, where AstraZeneca has filed similar motions to dismiss counterclaims directed to the '460 patent, and where a single arbiter will be assigned to preside over all pretrial matters.

II. PROCEDURAL BACKGROUND

On December 11, 2007, AstraZeneca sued Apotex Inc. and Apotex Corp. and six other generic drug manufacturing groups in the District of Delaware, alleging infringement of U.S. Reissue No. RE37,314 ("the '314 patent"), which claims the active ingredient, rosuvastatin calcium, in AstraZeneca's highly successful drug CRESTOR®. AstraZeneca also filed a mirror-image "protective suit" against one of the generic drug manufacturing groups, Aurobindo Pharma Ltd. and Aurobindo Pharma USA Inc. ("Aurobindo"), in the District of New Jersey. Aurobindo contested jurisdiction in Delaware, and answered the New Jersey complaint.

AstraZeneca's Delaware action against Apotex Inc. and Apotex Corp. resulted from their filing Abbreviated New Drug Application ("ANDA") No. 79-145 with the United States Food and Drug Administration ("FDA") to market generic versions of CRESTOR® before the '314 patent and the '460 patent expire—an act of patent infringement under 35 U.S.C. §

271(e)(2). AstraZeneca sued Apotex Inc. and Apotex Corp. for infringement of the '314 patent, but did not sue them, or any of the other defendants, for infringement of the '460 patent.

Instead of responding to the Delaware Complaint, Apotex Inc. contested the Delaware court's personal jurisdiction.[1] Discovery on Apotex Inc.'s motion to dismiss is currently underway, and the motion will be fully briefed by May 1, 2008.[2]

While contesting the Delaware court's jurisdiction over it, Apotex Inc. initiated this action in the Middle District of Florida. Here, Apotex Inc. seeks a declaratory judgment regarding the '460 patent—similar to declaratory judgment counterclaims filed by three defendant groups in Delaware concerning the '460 patent. Thus, the '460 patent is also at issue in Delaware.

On March 21, 2008, AstraZeneca moved to dismiss the counterclaims in the Delaware actions concerning the '460 patent. Since then, the '460 patent-related counterclaim of one of

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[1] Apotex Inc. challenged the Delaware court's personal jurisdiction, notwithstanding that in the past five years it has consented to that court's jurisdiction in eight prior litigations, at least one of which is still pending at very early stages. *See Boehringer Ingelheim Pharmaceuticals, Inc. v. Apotex Inc. et al.*, No. 08-065 (D.Del. filed February 21, 2008) (consenting to the Court's jurisdiction). *Sanofi-Aventis and Sanofi-Aventis U.S. LLC v. Apotex Inc. and Apotex Corp.*, No. 07-792 (D. Del. filed December 6, 2007); *Senju Pharm. Co., Ltd. et al.(including Allergan) v. Apotex Inc., Apotex Corp., and Apotex Pharm. India, PVT. Ltd.*, No. 07-779 (D. Del. filed November 29, 2007); *Allergan Inc. v. Apotex Inc. and Apotex Corp.*, No. 07-278 (D. Del. filed May 21, 2007); *MedPointe Healthcare Inc. v. Apotex Inc. and Apotex Corp.*, No. 07-204 (D. Del. filed April 17, 2007); *Merck & Co., Inc. v. Apotex Inc.*, No. 06-230 (D. Del. filed April 7, 2006); *MedPointe Healthcare v. Apotex Inc. and Apotex Corp.*, No. 06-164 (D. Del. filed March 10, 2006); *Apotex Inc. and Apotex Corp. v. Pfizer Inc.*, No. 03-990 (D. Del. filed October 29, 2003).

[2] Apotex Inc.'s subsidiary, Apotex Corp., also moved for dismissal, alleging that the Delaware court lacked subject matter jurisdiction over the patent infringement claims asserted by AstraZeneca against it.

the defendant groups, Cobalt Pharmaceuticals Inc. and Cobalt Laboratories Inc., was dismissed by stipulation. Briefing is still underway on AstraZeneca's motion to dismiss the '460 patent-related counterclaims of the other two defendant groups, Sandoz Inc. and Par Pharmaceutical, Inc.

On April 9, 2008, AstraZeneca similarly moved to dismiss this '460-patent action for lack of subject matter jurisdiction, because a covenant not to sue that AstraZeneca gave Apotex Inc. and Apotex Corp. eliminates the case or controversy between the parties regarding the '460 patent. Apotex Inc. nevertheless would not consent to that motion and has indicated that it intends to oppose AstraZeneca's motion based on a recent decision by the Federal Circuit, *Caraco Pharmaceutical Laboratories, Ltd. v. Forest Laboratories, Inc.*, No. 2007-1404, 2008 WL 850330 (Fed. Cir. April 1, 2008). *Caraco* held that in certain circumstances, not present here, a covenant not to sue does not eliminate a case or controversy. Apotex Inc., however, asserts a different view of the relevance of that case. Thus, an issue exists relating to the Court's subject matter jurisdiction over Apotex Inc.'s declaratory judgment action.

A month earlier, on March 13, 2008, AstraZeneca asked the JPMDL to transfer this action and the New Jersey action to Delaware pursuant to 28 U.S.C. § 1407 for coordinated pretrial proceedings. AstraZeneca made that request in view of the common factual and legal issues of the interrelated litigations, concerning, among other things, construction of the '460 patent's claims and its validity.[3] AstraZeneca's motion before the JPMDL will be fully

[3] Although Apotex Inc. has not asserted the defense of patent invalidity in its Complaint, it has not waived that defense, which under the permissive standards for amending pleadings could be readily added to the case. Moreover, in notifying AstraZeneca of its ANDA to the

(continued on next page)

briefed by the end of April. In response to AstraZeneca's transfer motion, the New Jersey Court *sua sponte* stayed the New Jersey action on March 26, 2008, pending the JPMDL ruling on consolidation. (Ex. A.)

In view of the likely ongoing litigation over the '460 patent with Apotex and two other defendant groups in Delaware, AstraZeneca moves to stay this action long enough to allow the JPMDL to resolve where pretrial proceedings concerning the '314 patent and the '460 patent should occur. In the meantime, Apotex Inc. has agreed to participate with the Delaware parties in setting a discovery schedule in Delaware, without prejudice to its motion to dismiss.[4] Moreover, if this action is stayed, AstraZeneca will provide discovery to Apotex Inc. on the '460 patent in the Delaware actions, even though Apotex has not formally asserted defenses in Delaware concerning that patent.

III. ARGUMENT

A. A Temporary Stay Will Promote Judicial Economy By Avoiding Duplicative Litigation

The Court should stay this action to allow time for the JPMDL to resolve AstraZeneca's transfer motion. This action shares common factual and legal issues with counterclaims brought by two defendant groups in Delaware concerning the '460 patent. Moreover, the '460 patent is directed to a formulation of rosuvastatin calcium and is, therefore, related to the '314 patent that is directed to rosuvastatin calcium itself. Both patents

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FDA, Apotex Inc. alleged that its generic CRESTOR® product would not infringe the '460 patent and expressly reserved the right to assert the defense of patent invalidity.

[4] The Delaware court held its scheduling conference on April 10, 2008, and the scheduling order is expected in the near future. The court set a trial date for February 2010.

cover AstraZeneca's commercial CRESTOR® product. Thus, the discovery in both cases will overlap.

"It is common practice for courts to stay an action pending a transfer decision by the [JPMDL]." *Bonenfant v. R.J. Reynolds Tobacco Co.,* No. 07-60301-CIV, 2007 WL 2409980, at *1 (S.D. Fla. July 31, 2007) (citing *Republic of Venezuela v. Philip Morris Cos., Inc.,* No. 99-0586-CIV, 1999 WL 33911677 (S.D. Fla. April 28, 1999)). The court in *Republic of Venezuela,* succinctly stated the standard for deciding such a motion:

> A district court has the discretion to stay its proceedings. This power is derived from and incidental to a court's inherent power to control the disposition of cases on its docket and ensure a 'fair and efficient' adjudication of matters. *See Gold v. Johns-Manville Sales Corp.,* 723 F.2d 1068, 1077 (3d Cir. 1983). *See also Landis v. North Am. Co.,* 229 U.S. 248, 254 (1936). If granting the stay prejudices the non-movant, the movant must clearly demonstrate hardship or inequity. *See Gold,* 723 at 1076.

*Republic of Venezuela,*1999 WL 33911677, at *1.

Under circumstances similar to these, the *Bonenfant* court granted a motion to stay while the transfer motion was pending before the JPMDL. As here, the *Bonenfant* court determined that the related actions likely shared common questions of law and fact, that jurisdictional questions were before the transferee court, and that the JPDML would likely grant the motion to transfer.[5]

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[5] There is compelling precedent for the JPMDL to grant AstraZeneca's transfer motion. *See In re Amoxicillin Patent and Antitrust Litig.*, 449 F. Supp. 601, 603 (J.P.M.L. 1978) ("the strong likelihood that discovery concerning these questions will be both complicated and time-consuming."); *In re Desloratadine*, 502 F. Supp.2d at 1355-56 ("expected to share factual questions with respect to the [] patent's validity and enforceability, among other things" in the district that "already encompasses all defendants, and [where] the common party patent holder is located"); *In re Metoprolol,* 329 F. Supp.2d at 1369-70 (validity of two complex pharmaceutical patents); *In re FMC Corporation Patent Litigation*, 422 F. Supp.

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The Manual for Complex Litigation provides additional support for staying the action. It provides that a "stay pending the Panel's decision can increase efficiency and consistency, particularly when the transferor court believes that a transfer order is likely and when the pending motions raise issues likely to be raised in other cases as well." Manual for Complex Litigation (Fourth) § 22.35 (2005).

B. Neither Apotex Nor the Public Will Be Prejudiced

Neither Apotex Inc. nor the public will be harmed by the entry of a stay. Apotex Inc. is already voluntarily participating in pretrial proceedings in Delaware, without prejudice to its motion to dismiss for lack of personal jurisdiction. AstraZeneca moves only for a temporary stay of these proceedings, pending resolution of proceedings before the JPMDL. In the meantime, Apotex Inc. will be fruitfully engaged in Delaware discovery, concerning, among other things, the '460 patent that it can use in this action, if necessary, and will suffer no prejudice. Moreover, a stay will further the public interest by avoiding duplication of judicial effort, while permitting pretrial proceedings on the '460 patent to go forward in a coordinated manner in Delaware.

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1163, 1165 (J.P.M.L. 1976) (patent litigations "involv[ing] common factual questions concerning the validity of the patent."); *In re Pharmastem Therapeutics, Inc., Patent Litig.*, 360 F. Supp. 2d 1362, 1364 (J.P.M.L. 2005) (patent actions "expected to share factual and legal questions concerning such matters as the technology underlying the patents, prior art, claim construction and issues of infringement involving the patents."); *In re Phonometrics, Inc., Elec. Long Dist. Call Cost Computer and Recorder Patent Lit.*, 1997 WL 83673, *1 (J.P.M.L. 1997) (21 separate actions that "will likely share questions concerning such matters as patent validity, prior art, obviousness and interpretation of the claims of the patent").

IV. CONCLUSION

For the foregoing reasons, the Court should grant the requested temporary stay.

LOCAL RULE 3.01(g) CERTIFICATION

Counsel for Defendants has conferred with counsel for Plaintiff; however, the parties have been unable to reach an agreement as to the requested relief.

Dated: April 11, 2008

Respectfully submitted,

s/Lara J. Tibbals
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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on April 11, 2008, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to Lee Fugate and Nathan M. Berman, Zuckerman Spaeder LLP, 101 E. Kennedy Boulevard, Suite 1200, Tampa, Florida 33602 and to Robert B. Breisblatt, Katten Muchin Rosenman, LLP, 525 West Monroe Street, Chicago, Illinois 60661-3693, and to J. Aron Carnahan and Laurie A. Haynie, Welsh & Katz, Ltd., 120 S. Riverside Plaza, 22nd Floor, Chicago, Illinois 60606.

s/Lara J. Tibbals
Attorney

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ASTRAZENECA PHARMACEUTICALS LP, et al.,	CIVIL ACTION NO. 07-6020 (MLC)
Plaintiffs,	**O R D E R**
v.	
AUROBINDO PHARMA LIMITED, et al.,	
Defendants.	

IT APPEARING that a motion pursuant to 28 U.S.C. § 1407 to transfer this action is pending before the United States Judicial Panel on Multidistrict Litigation ("Panel"), see In re: Rosuvastatin Calcium Patent Litig., MDL No. 1949, 3-17-08 Notification; and the Court having the inherent power to control the docket, Landis v. N. Am. Co., 299 U.S. 248, 254 (1936), Rolo v. Gen. Dev. Corp., 949 F.2d 695, 702 (3d Cir. 1991); and the Court determining that the interests of judicial economy will be best served by staying this action pending the final outcome of the proceedings before the Panel; and for good cause appearing;

IT IS THEREFORE on this 26th day of March, 2008 **ORDERED** that – with the exception of the pending motions to seal (dkt. entry nos. 25 & 34), which shall remain within the province of the Magistrate Judge – all further proceedings in this action, including but not limited to the submission of any new or additional motions or briefing and the submission of any further pleadings or answers, are **STAYED** pending the final outcome of the proceedings before the United States Judicial Panel on Multidistrict Litigation; and

IT IS FURTHER ORDERED that the defendants' motion to dismiss (dkt. entry no. 6) is **DENIED WITHOUT PREJUDICE**, and with leave to move again when the stay is lifted; and

IT IS FURTHER ORDERED that the plaintiffs' cross motion to stay (dkt. entry no. 20) is **DENIED WITHOUT PREJUDICE AS MOOT.**

s/ Mary L. Cooper
MARY L. COOPER
United States District Judge

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC., Plaintiff, v. ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC. Defendants.	Civil Action No. 8:08:cv-213-JSM-TGW

UNOPPOSED MOTION FOR ENLARGEMENT OF TIME

Plaintiff Apotex Inc. and Defendants AstraZeneca Pharmaceuticals, LP, AstraZeneca UK Limited, and IPR Pharmaceuticals, Inc. ("Defendants") move this Court to enter an order enlarging the time within which Plaintiff must respond to Defendants' Motion to Dismiss, which was filed on April 11, 2008 (Docket No. 15), as follows:

1. Absent an enlargement of time, Plaintiff's Response to Defendants' Motion to Dismiss is due on April 28, 2008.

2. After filing their Motion to Dismiss, Defendants filed a Motion for a Temporary Stay pending a decision by the Judicial Panel on Multidistrict Litigation. (Docket No. 16.) Plaintiff has since agreed to the Motion to Stay.

3. In the event Defendants' Motion to Stay is granted, the parties request an extension of 30 days until after the stay is lifted for Plaintiff to respond to Defendants' Motion to Dismiss.

4. In the event Defendants' Motion to Stay is denied, the parties request an extension of time until 30 days after the ruling denying the motion to stay for Plaintiff to respond to Defendants' Motion to Dismiss.

5. Defendants have indicated that they agree to the granting of such an enlargement of time.

WHEREFORE Plaintiff and Defendants respectfully request this Court enter an order enlarging the time within which Plaintiff must respond to Defendants' Motion to Dismiss as set forth herein.

LOCAL RULE 3.01(g) CERTIFICATION

Counsel for Plaintiff has conferred with counsel for Defendants, and counsel for Defendants agree to the granting of the relief requested herein.

Dated: April 18, 2008

Respectfully submitted,

/s/ Lee Fugate
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Of Counsel for Plaintiff Apotex Inc.

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v. Case No.: 8:08-cv-213-JSM-TGW

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.
_____/

NOTICE OF PLAINTIFF'S JOINDER IN DEFENDANTS' MOTION FOR TEMPORARY STAY

Defendants, ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC., hereby give notice that Plaintiff joins in and consents to the relief sought in Defendants' Motion for a Temporary Stay (Dkt. No. 16). Accordingly, the parties hereby jointly move this Court to stay this action, pending a decision by the Judicial Panel on Multidistrict Litigation on Astrazeneca's Motion to transfer this and a related action to Delaware for coordinated pretrial proceedings.

Respectfully submitted,

s/William C. Guerrant, Jr.
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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on April 21, 2008, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to Lee Fugate and Nathan M. Berman, Zuckerman Spaeder LLP, 101 E. Kennedy Boulevard, Suite 1200, Tampa, Florida 33602 and to Robert B. Breisblatt, Katten Muchin Rosenman, LLP, 525 West Monroe Street, Chicago, Illinois 60661-3693, and to J. Aron Carnahan and Laurie A. Haynie, Welsh & Katz, Ltd., 120 S. Riverside Plaza, 22nd Floor, Chicago, Illinois 60606.

s/William C. Guerrant, Jr.
Attorney

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

APOTEX INC.,

Plaintiff,

v. Case No.: 8:08-cv-213-JSM-TGW

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC.,

Defendants.
_____/

NOTICE OF TRANSFER TO MULTIDISTRICT LITIGATION

Defendants, AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, and IPR Pharmaceuticals, Inc., by and through undersigned counsel, and pursuant to this Court's Order granting Defendants' Motion to Stay dated April 22, 2008 (Dkt. #19), hereby notify the Court that this action has been transferred to the District of Delaware by the Judicial Panel on Multidistrict Litigation by Order dated June 13, 2008. A copy of the Order of Transfer is attached hereto as Exhibit "A."

Respectfully submitted,

s/Lara J. Tibbals
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Lara J. Tibbals, FBN 129054
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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on June 17, 2008, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to Lee Fugate and Nathan M. Berman, Zuckerman Spaeder LLP, 101 E. Kennedy Boulevard, Suite 1200, Tampa, Florida 33602 and to Robert B. Breisblatt, Katten Muchin Rosenman, LLP, 525 West Monroe Street, Chicago, Illinois 60661-3693, and to J. Aron Carnahan and Laurie A. Haynie, Welsh & Katz, Ltd., 120 S. Riverside Plaza, 22nd Floor, Chicago, Illinois 60606.

s/Lara J. Tibbals
Attorney

606677

UNITED STATES JUDICIAL PANEL
on
MULTIDISTRICT LITIGATION

IN RE: ROSUVASTATIN CALCIUM PATENT LITIGATION

MDL No. 1949

TRANSFER ORDER

Before the entire Panel: Plaintiffs AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals, Inc., and Shionogi Seiyaku Kabushiki Kaisha (collectively AstraZeneca) have moved, pursuant to 28 U.S.C. § 1407, to centralize this litigation in the District of Delaware. This litigation currently consists of nine actions, seven actions in the District of Delaware and one action each in the District of New Jersey and the Middle District of Florida, as listed on Schedule A.

Mylan Pharmaceuticals Inc., which is a defendant in one of the Delaware actions, supports centralization, but asks that the Panel select either the District of New Jersey or the Middle District of Florida as transferee district. Aurobindo Pharma Limited and Aurobindo Pharma USA, Inc. (collectively Aurobindo), which are defendants in one of the Delaware actions and the New Jersey action, oppose centralization, as do Apotex Inc. and Apotex Corp. (collectively Apotex), which are defendants in one of the Delaware actions and plaintiffs in the Florida action. If the Panel orders centralization over these parties' objections, then Apotex urges that the Panel select the Middle District of Florida as transferee district, while Aurobindo asks that the Panel select a district with more favorable docket conditions than the District of Delaware.

On the basis of the papers filed and hearing session held, we find that these nine actions involve common questions of fact, and that centralization under Section 1407 will serve the convenience of the parties and witnesses and promote the just and efficient conduct of the litigation. All nine actions involve common factual allegations concerning U.S. Patent Nos. RE37,314 (the '314 patent) or 6,316,460 (the '460 patent), which are both listed in the Food and Drug Administration's register of pharmaceutical patents for AstraZeneca's Crestor drug. Centralization under Section 1407 will eliminate duplicative discovery, prevent inconsistent pretrial rulings (particularly on claim construction issues), and conserve the resources of the parties, their counsel and the judiciary.

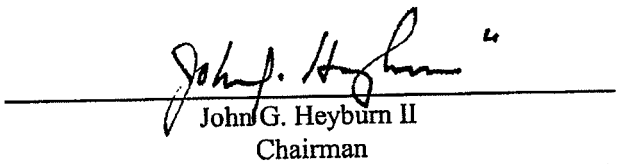
In opposition to centralization, Aurobindo and Apotex argue that alternatives to centralization are both available and preferable, and Apotex contends that the Florida lawsuit is a straightforward action involving only a declaratory judgment claim for non-infringement as to the '460 patent. Based upon the Panel's precedents and for the following reasons, we respectfully disagree with these arguments. Actions involving the validity of complex pharmaceutical patents and the entry of generic versions of the patentholder's drugs are particularly well-suited for transfer under Section 1407. *See, e.g., In re Brimonidine Patent Litigation,* 507 F.Supp.2d 1381, 1382 (J.P.M.L. 2007). The two patents

at issue both relate to AstraZeneca's Crestor drug, and centralization will place all actions in this docket before a single judge who can structure pretrial proceedings to accommodate all parties' legitimate discovery needs while ensuring that the common parties and witnesses are not subjected to discovery demands that duplicate activity that will or has occurred in other actions. *See In re Department of Veterans Affairs (VA) Data Theft Litigation*, 461 F.Supp.2d 1367, 1368-69 (J.P.M.L. 2006). Discovery with respect to any case-specific issues can also proceed concurrently with discovery on common issues. *See id.*

We are persuaded that the District of Delaware is an appropriate transferee district for pretrial proceedings in this litigation. Seven of the nine actions, including the first-filed actions, are already pending in that district, and in assigning the litigation to Judge Joseph J. Farnan, Jr. (who is already overseeing the seven Delaware actions), we are entrusting the docket to a jurist who has the experience to steer it on a prudent course.

IT IS THEREFORE ORDERED that, pursuant to 28 U.S.C. § 1407, the two actions listed on Schedule A and pending outside the District of Delaware are transferred to the District of Delaware and, with the consent of that court, assigned to the Honorable Joseph J. Farnan, Jr., for coordinated or consolidated pretrial proceedings with the actions pending in that district and listed on Schedule A.

PANEL ON MULTIDISTRICT LITIGATION



John G. Heyburn II
Chairman

D. Lowell Jensen
Robert L. Miller, Jr.
David R. Hansen

J. Frederick Motz
Kathryn H. Vratil
Anthony J. Scirica

IN RE: ROSUVASTATIN CALCIUM PATENT LITIGATION

MDL No. 1949

SCHEDULE A

District of Delaware

AstraZeneca Pharmaceuticals, LP, et al. v. Mylan Pharmaceuticals, Inc., C.A. No. 1:07-805
AstraZeneca Pharmaceuticals, LP, et al. v. Sun Pharmaceutical Industries, Ltd., et al., C.A. No. 1:07-806
AstraZeneca Pharmaceuticals, LP, et al. v. Sandoz, Inc., C.A. No. 1:07-807
AstraZeneca Pharmaceuticals, LP, et al. v. Par Pharmaceutical, Inc., C.A. No. 1:07-808
AstraZeneca Pharmaceuticals, LP, et al. v. Apotex, Inc., et al., C.A. No. 1:07-809
AstraZeneca Pharmaceuticals, LP, et al. v. Aurobindo Pharma Ltd., et al., C.A. No. 1:07-810
AstraZeneca Pharmaceuticals, LP, et al. v. Cobalt Pharmaceuticals, Inc., et al., C.A. No. 1:07-811

Middle District of Florida

Apotex, Inc. v. AstraZeneca Pharmaceuticals, LP, et al., C.A. No. 8:08-213

District of New Jersey

AstraZeneca Pharmaceuticals, LP, et al. v. Aurobindo Pharma Ltd., et al., C.A. No. 3:07-6020

8:08CV213

UNITED STATES JUDICIAL PANEL
on
MULTIDISTRICT LITIGATION

IN RE: ROSUVASTATIN CALCIUM PATENT LITIGATION

MDL No. 1949

TRANSFER ORDER

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Mylan Pharmaceuticals Inc., which is a defendant in one of the Delaware actions, supports centralization, but asks that the Panel select either the District of New Jersey or the Middle District of Florida as transferee district. Aurobindo Pharma Limited and Aurobindo Pharma USA, Inc. (collectively Aurobindo), which are defendants in one of the Delaware actions and the New Jersey action, oppose centralization, as do Apotex Inc. and Apotex Corp. (collectively Apotex), which are defendants in one of the Delaware actions and plaintiffs in the Florida action. If the Panel orders centralization over these parties' objections, then Apotex urges that the Panel select the Middle District of Florida as transferee district, while Aurobindo asks that the Panel select a district with more favorable docket conditions than the District of Delaware.

On the basis of the papers filed and hearing session held, we find that these nine actions involve common questions of fact, and that centralization under Section 1407 will serve the convenience of the parties and witnesses and promote the just and efficient conduct of the litigation. All nine actions involve common factual allegations concerning U.S. Patent Nos. RE37,314 (the '314 patent) or 6,316,460 (the '460 patent), which are both listed in the Food and Drug Administration's register of pharmaceutical patents for AstraZeneca's Crestor drug. Centralization under Section 1407 will eliminate duplicative discovery, prevent inconsistent pretrial rulings (particularly on claim construction issues), and conserve the resources of the parties, their counsel and the judiciary.

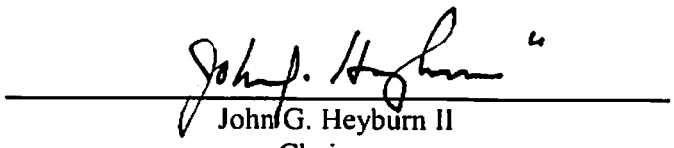
In opposition to centralization, Aurobindo and Apotex argue that alternatives to centralization are both available and preferable, and Apotex contends that the Florida lawsuit is a straightforward action involving only a declaratory judgment claim for non-infringement as to the '460 patent. Based upon the Panel's precedents and for the following reasons, we respectfully disagree with these arguments. Actions involving the validity of complex pharmaceutical patents and the entry of generic versions of the patentholder's drugs are particularly well-suited for transfer under Section 1407. *See, e.g., In re Brimonidine Patent Litigation,* 507 F.Supp.2d 1381, 1382 (J.P.M.L. 2007). The two patents

at issue both relate to AstraZeneca's Crestor drug, and centralization will place all actions in this docket before a single judge who can structure pretrial proceedings to accommodate all parties' legitimate discovery needs while ensuring that the common parties and witnesses are not subjected to discovery demands that duplicate activity that will or has occurred in other actions. *See In re Department of Veterans Affairs (VA) Data Theft Litigation*, 461 F.Supp.2d 1367, 1368-69 (J.P.M.L. 2006). Discovery with respect to any case-specific issues can also proceed concurrently with discovery on common issues. *See id.*

We are persuaded that the District of Delaware is an appropriate transferee district for pretrial proceedings in this litigation. Seven of the nine actions, including the first-filed actions, are already pending in that district, and in assigning the litigation to Judge Joseph J. Farnan, Jr. (who is already overseeing the seven Delaware actions), we are entrusting the docket to a jurist who has the experience to steer it on a prudent course.

IT IS THEREFORE ORDERED that, pursuant to 28 U.S.C. § 1407, the two actions listed on Schedule A and pending outside the District of Delaware are transferred to the District of Delaware and, with the consent of that court, assigned to the Honorable Joseph J. Farnan, Jr., for coordinated or consolidated pretrial proceedings with the actions pending in that district and listed on Schedule A.

PANEL ON MULTIDISTRICT LITIGATION



John G. Heyburn II
Chairman

D. Lowell Jensen
Robert L. Miller, Jr.
David R. Hansen

J. Frederick Motz
Kathryn H. Vratil
Anthony J. Scirica

IN RE: ROSUVASTATIN CALCIUM PATENT LITIGATION MDL No. 1949

SCHEDULE A

District of Delaware

AstraZeneca Pharmaceuticals, LP, et al. v. Mylan Pharmaceuticals, Inc., C.A. No. 1:07-805
AstraZeneca Pharmaceuticals, LP, et al. v. Sun Pharmaceutical Industries, Ltd., et al., C.A. No. 1:07-806
AstraZeneca Pharmaceuticals, LP, et al. v. Sandoz, Inc., C.A. No. 1:07-807
AstraZeneca Pharmaceuticals, LP, et al. v. Par Pharmaceutical, Inc., C.A. No. 1:07-808
AstraZeneca Pharmaceuticals, LP, et al. v. Apotex, Inc., et al., C.A. No. 1:07-809
AstraZeneca Pharmaceuticals, LP, et al. v. Aurobindo Pharma Ltd., et al., C.A. No. 1:07-810
AstraZeneca Pharmaceuticals, LP, et al. v. Cobalt Pharmaceuticals, Inc., et al., C.A. No. 1:07-811

Middle District of Florida

Apotex, Inc. v. AstraZeneca Pharmaceuticals, LP, et al., C.A. No. 8:08-213

District of New Jersey

AstraZeneca Pharmaceuticals, LP, et al. v. Aurobindo Pharma Ltd., et al., C.A. No. 3:07-6020

CERTIFIED: 6/16/08
AS A TRUE COPY:
ATTEST:
PETER T. DALLEO, CLERK
BY Elsa A. Diaz
Deputy Clerk